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TO: Tamthom Truong Location: REM-5B19/5C18 Art Unit: 1624 Tuesday, November 29, 2005 Case Serial Number: 10/613782	From: Mary Hale Location: Biotech/Chem Library Rem 1D86 Phone: 2-2507 Mary.Hale@uspto.gov

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171578

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2-m amdt

Your Contact Information:
* indicates mandatory information.

Your Name: TAMTHOM TRUONG
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*Art Unit/Org.: 1624
*Office Location: REM -- 5B19
*Phone No.: x 20676
Mailbox No.: REM -- 5C18

***Case serial number:** 10/ 613,782
If not related to a patent application, please enter NA here.

Class / Subclass(es) 514/ 266.1; 544/ 284

Earliest Priority Filing Date: 07-05-02

Format preferred for results:
☑ Paper ☐ Diskette ☐ E-mail

Provide detailed information on your search topic:

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- Include synonyms, keywords, and acronyms. Define terms that have special me
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  Include the elected species or structures, keywords, synonyms, acronyms, and
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Bib Data Sheet

CONFIRMATION NO. 6985

SERIAL NUMBER	FILING DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
10/613,782	07/03/2003 RULE	514	1624	21159

APPLICANTS

Patrizio Mattei, Riehen, SWITZERLAND;

Werner Mueller, Aesch, SWITZERLAND;
Werner Neidhart, Hagenthal le Bas, FRANCE;Matthias Heinrich Nettekoven, Grenzach-Wyhlen, GERMANY;
Philippe Pflieger, Schwoben, FRANCE;

** CONTINUING DATA **********

** FOREIGN APPLICATIONS **********
EUROPEAN PATENT OFFICE (EPO) 02014904.3 07/05/2002

IF REQUIRED, FOREIGN FILING LICENSE GRANTED
** 10/27/2003

Foreign Priority claimed ☐ yes ☐ no 35 USC 119 (a-d) conditions met ☐ yes ☐ no ☐ Met after Allowance Verified and Acknowledged Examiner's Signature Initials	STATE OR COUNTRY SWITZERLAND	SHEETS DRAWING 0	TOTAL CLAIMS 18	INDEPENDENT CLAIMS 1

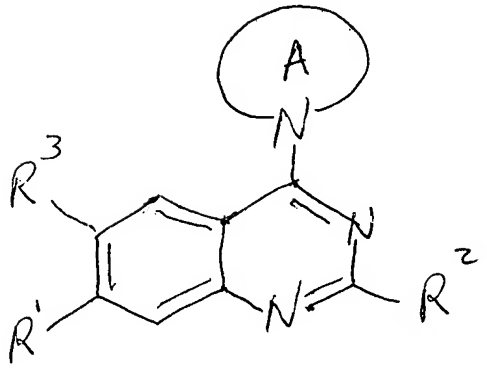
ADDRESS
000151
HOFFMANN-LA ROCHE INC.
PATENT LAW DEPARTMENT
340 KINGSLAND STREET
NUTLEY , NJ
07110

TITLE
Quinazoline derivatives

☐ All Fees
☐ 1.16 Fees (Filing)

FILING FEE RECEIVED 750	FEES: Authority has been given in Paper No. _____ to charge/credit DEPOSIT ACCOUNT No. _____ for following:	☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit

10/613,782 Query



R^1 = $-OR^4$ or $-N(R^5)(R^6)$

R^2 = Alkyl or amino

R^3 = H, Alkyl or halogen

R^4 = hydrogen or (Ring)$-(CH_2)_{0-7}$

R^5, R^6 = H, (Ring)$-(CH_2)_{0-7}$,

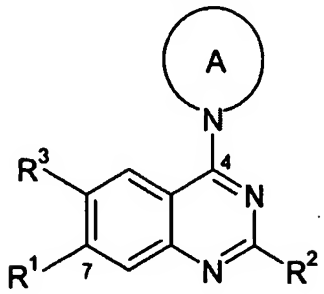
or, (Het)$-C(=O)-$,

or $R^5 + R^6$ = forming a ring w/ the nitrogen they're attached to.

See also attached claims 1 & 13.

In the Claims:

1. (Currently Amended) A compound of formula I



I

wherein

R^1 is -O-R^4 or -N(R^5)(R^6);

R^2 is alkyl or amino;

R^3 is hydrogen, alkyl or halogen;

R^4 is hydrogen, aralkyl, substituted aralkyl, heterocyclylalkyl, substituted heterocyclylalkyl or cycloalkylalkyl;~~hydrogen,~~

~~alkyl,~~

~~alkoxyalkyl,~~

~~hydroxyalkyl,~~

~~aralkyl,~~

~~aralkyl which is substituted on the aryl with one or more substituents independently selected from halogen, trifluoromethyl, amino, alkyl, alkoxy, alkylcarbonyl, cyano, carbamoyl, alkoxycarbamoyl, methylendioxy, carboxy, alkoxycarbonyl, aminocarbonyl, alkyaminocarbonyl, dialkylaminocarbonyl and hydroxy,~~

~~heterocyclylalkyl,~~

~~heterocyclylalkyl which is substituted on one or more carbon atoms of the heterocyclyl by one or more substituents independently selected from halogen, alkyl, alkoxy, oxo, cyano and haloalkyl,~~

~~cycloalkylalkyl,~~

~~amino-SO_2-, or~~

~~alkyl-SO_2-;~~

R^5 and R^6 are independently selected from hydrogen, alkyl, cycloalkylalkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heterocyclyl, substituted heterocyclyl, heterocyclylcarbonyl or substituted heterocyclylcarbonyl~~hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, alkylcarbonyl, cycloalkylcarbonyl, aryl, aryl which is substituted with one or more substituents independently selected from halogen, trifluoromethyl, amino, alkyl, alkoxy, alkylcarbonyl, cyano, carbamoyl, alkoxycarbamoyl, methylendioxy, carboxy, alkoxycarbonyl, aminocarbonyl, alkyaminocarbonyl, dialkylaminocarbonyl, hydroxy and nitro; aralkyl, substituted aralkyl, arylcarbonyl, substituted arylcarbonyl, alkoxyalkyl, hydroxyalkyl, heterocyclyl, heterocyclyl which is substituted on one or more carbon atoms by one or more substituents independently selected from halogen, alkyl, alkoxy, oxo, cyano and haloalkyl; heterocyclylalkyl, substituted heterocyclylalkyl, heterocyclylcarbonyl, substituted heterocyclylcarbonyl, alkyl-SO_2-, aryl-SO_2-, heterocyclyl-SO_2-, substituted heterocyclyl-SO_2-, or amino-SO_2-, wherein substituted heterocyclylalkyl, substituted heterocyclylcarbonyl, and heterocyclyl-SO_2- are each substituted on one or more carbon atoms of the heterocyclyl by one or more substituents independently selected from halogen, alkyl, alkoxy, oxo, cyano and haloalkyl, and wherein substituted aralkyl and substituted arylcarbonyl are each substituted on the aryl with one or more substituents independently selected from halogen, trifluoromethyl, amino, alkyl, alkoxy, alkylcarbonyl, cyano, carbamoyl, alkoxycarbamoyl, methylendioxy, carboxy, alkoxycarbonyl, aminocarbonyl, alkyaminocarbonyl, dialkylaminocarbonyl, hydroxy and nitro~~, or

R^5 and R^6 together with the N atom to which they are attached form a 5- to 10- membered unsubstituted or substituted heterocyclic ring which optionally comprises a second heteroatom selected from nitrogen or oxygen and, wherein the substituted heterocyclyl ring has one or more substituents independently selected from alkyl and alkoxy;

A is a 5 to 7-membered saturated unsubstituted or substituted heterocyclic ring comprising the nitrogen atom which is attached to the quinazoline ring and optionally a second heteroatom which is selected from oxygen, sulfur or nitrogen and, wherein the ring A substituted heterocyclic ring has one or more substituents independently selected from halogen, alkyl, alkoxy, haloalkoxy, cycloalkylalkoxy, hydroxy, amino, acetylamino, cyano, hydroxyalkyl, alkoxyalkyl, haloalkoxyalkyl and cycloalkylalkoxyalkyl;

and pharmaceutically acceptable salts and esters thereof.

13. (Original) The compound according to claim 1 selected from
4-(2-Methyl-4-pyrrolidin-1-yl-quinazolin-7-yloxymethyl)-benzonitrile;
7-(2-Chloro-pyridin-3-ylmethoxy)-2-methyl-4-pyrrolidin-1-yl-quinazoline;
7-(2-Fluoro-pyridin-3-ylmethoxy)-2-methyl-4-pyrrolidin-1-yl-quinazoline;
(S)-{1-[7-(2-Chloro-pyridin-3-ylmethoxy)-2-methyl-quinazolin-4-yl]-pyrrolidin-2-yl}-methanol;
(S)-4-[4-(3-Ethoxy-pyrrolidin-1-yl)-2-methyl-quinazolin-7-yloxymethyl]-benzonitrile;
Isobutyl-(2-methyl-4-pyrrolidin-1-yl-quinazolin-7-yl)-amine;
(2-Methyl-4-pyrrolidin-1-yl-quinazolin-7-yl)-pyridin-3-yl-amine;
Furan-2-carboxylic acid (2-methyl-4-pyrrolidin-1-yl-quinazolin-7-yl)-amide;
(S)-[4-(3-Ethoxy-pyrrolidin-1-yl)-2-methyl-quinazolin-7-yl]-pyridin-3-yl-amine; and
(S)-[4-(3-Methoxy-pyrrolidin-1-yl)-2-methyl-quinazolin-7-yl]-pyridin-3-yl-amine.

14. (Original) A pharmaceutical composition comprising a therapeutically effective amount of a compound in accordance with claim 1 and a pharmaceutically acceptable carrier.

15. (Original) A method of treatment of obesity in a patient in need of such treatment which comprises administering to the patient a therapeutically effective amount of from about 0.1 mg to 20 mg per kg body weight per day of the compound according to claim 1.

16. (Original) A method of treatment of obesity in a patient in need of such treatment which comprises administering to the patient a therapeutically effective amount from about 0.1 mg to 20 mg per kg body weight per day of the compound according to claim 1 and a therapeutically effective amount of from 60 to 720 mg per day of orlistat.

17. (Original) The method according to claim 16 wherein the compound according to claim 1 and the orlistat are administered simultaneously, separately or sequentially.

NGO
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(FILE 'HOME' ENTERED AT 10:57:04 ON 29 NOV 2005)

FILE 'REGISTRY' ENTERED AT 10:57:13 ON 29 NOV 2005
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L3 39 S L1 FUL

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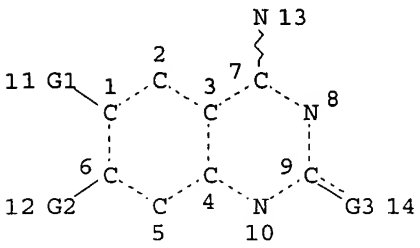
L1 STR



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VAR G2=O/N
VAR G3=C/N
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NSPEC IS R AT 13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
L3 39 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED 12672 ITERATIONS 39 ANSWERS
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FULL ESTIMATED COST	162.62	162.83

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FILE 'EMBASE' ENTERED AT 10:59:48 ON 29 NOV 2005

FILE 'CAPLUS' ENTERED AT 10:59:48 ON 29 NOV 2005

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

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L4            0 FILE MEDLINE
L5            0 FILE BIOSIS
L6            0 FILE EMBASE
L7            4 FILE CAPLUS

TOTAL FOR ALL FILES
L8            4 L3

=> d 1-4 ibib abs hitstr

L8   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:41451  CAPLUS
DOCUMENT NUMBER:          140:111423
TITLE:                    Quinazoline derivatives useful as neuropeptide Y (NPY)
                          receptor ligands, particularly antagonists, their
                          preparation and pharmaceutical compositions, and their
                          use in the treatment of, e.g. obesity
INVENTOR(S):              Mattei, Patrizio; Mueller, Werner; Neidhart, Werner;
                          Nettekoven, Matthias Heinrich; Pflieger, Philippe
PATENT ASSIGNEE(S):       F. Hoffmann-La Roche Ag, Switz.
SOURCE:                   PCT Int. Appl., 44 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    -------------------      --------
     WO 2004005265         A1    20040115    WO 2003-EP6868           20030627
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
             UG, UZ, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2489251            AA    20040115    CA 2003-2489251          20030627
     BR 2003012461         A     20050426    BR 2003-12461            20030627
     EP 1560816            A1    20050810    EP 2003-740372           20030627
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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     JP 2005535648         T2    20051124    JP 2004-518609           20030627
     US 2004029901         A1    20040212    US 2003-613782           20030703
PRIORITY APPLN. INFO.:                       EP 2002-14904        A   20020705
                                             WO 2003-EP6868       W   20030627
OTHER SOURCE(S):          MARPAT 140:111423
GI
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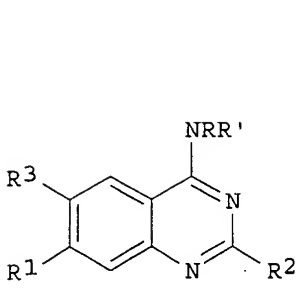

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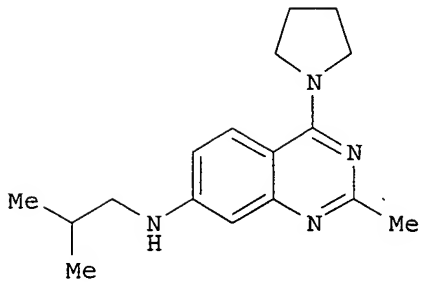


II

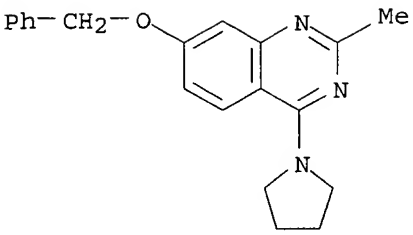
AB Title compds. I and their pharmaceutically acceptable salts and esters can be used in the form of pharmaceutical prepns. for the treatment or prevention of arthritis, cardiovascular diseases, diabetes, renal failure, eating disorders, and obesity [wherein: R1 = OR4 or NR5R6; = alkyl or amino; R3 = H, alkyl, or halogen; R4 = H, alkyl, alkoxyalkyl, hydroxyalkyl, aralkyl, heterocyclylalkyl, cycloalkylalkyl, amino-SO2-, or alkyl-SO2-; R5, R6 = H, alkyl, cycloalkyl, cycloalkylalkyl, alkylcarbonyl, cycloalkylcarbonyl, aryl, aralkyl, arylcarbonyl, alkoxyalkyl, hydroxyalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, alkyl-SO2-, aryl-SO2-, heterocyclyl-SO2-, or amino-SO2-; or NR5R6 = 5- to 10-membered heterocyclic ring with optional addnl. N or O atom, and optionally substituted with alkyl and/or alkoxy; NRR' = 5- to 7-membered saturated heterocyclic ring optionally containing a second heteroatom (O, N, or S)
and, optionally substituted by halogen, alkyl, alkoxy, haloalkoxy, cycloalkylalkoxy, hydroxy, amino, acetylamino, cyano, hydroxyalkyl, alkoxyalkyl, haloalkoxyalkyl, and cycloalkylalkoxyalkyl]. I are neuropeptide ligands; more specifically, they are selective neuropeptide Y (NPY) antagonists, and in particular, they are antagonists for the Y5 receptor subtype. Approx. 34 specific examples were prepared, and 10 of these are claimed. For instance, 4-bromoanthranilic acid was cyclocondensed with acetyl chloride to give 99.4% 7-bromo-2-methyl-3H-quinazolin-4-one, which was treated with POCl3 and PhNMe2 to give 59% 7-bromo-4-chloro-2-methylquinazoline. Aminolysis of this dihalide, first with pyrrolidine at the 4-position (100%), and then with isobutylamine at the 7-position, gave a preferred invention compound, II. In tests for displacement of labeled peptide YY (PYY) from mouse brain NPY5 receptors expressed in HEK 293 cells, compound II had an IC50 value of 3 nM.

IT **646450-52-4P**, 7-Benzyloxy-2-methyl-4-pyrrolidin-1-ylquinazoline
646450-53-5P, 2-Methyl-4-pyrrolidin-1-ylquinazolin-7-ol
646450-66-0P, (S)-[1-(7-Benzyloxy-2-methylquinazolin-4-yl)pyrrolidin-2-yl]methanol **646450-67-1P**, (S)-4-(2-Hydroxymethylpyrrolidin-1-yl)-2-methylquinazolin-7-ol **646450-73-9P**, (S)-7-Benzyloxy-4-(3-ethoxypyrrolidin-1-yl)-2-methylquinazoline **646450-74-0P**, (S)-4-(3-Ethoxypyrrolidin-1-yl)-2-methylquinazolin-7-ol **646450-76-2P**, (S)-1-(7-Benzyloxy-2-methylquinazolin-4-yl)pyrrolidin-3-ol **646450-77-3P**, (S)-4-(3-Hydroxypyrrolidin-1-yl)-2-methylquinazolin-7-ol
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of quinazoline derivs. as NPY antagonists for treatment of obesity, etc.)

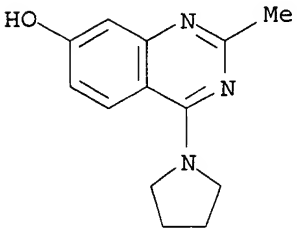
RN 646450-52-4 CAPLUS

CN Quinazoline, 2-methyl-7-(phenylmethoxy)-4-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

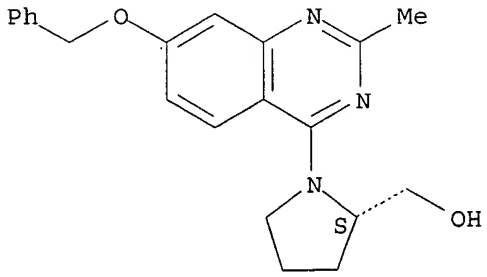


RN 646450-53-5 CAPLUS
CN 7-Quinazolinol, 2-methyl-4-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



RN 646450-66-0 CAPLUS
CN 2-Pyrrolidinemethanol, 1-[2-methyl-7-(phenylmethoxy)-4-quinazolinyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 646450-67-1 CAPLUS
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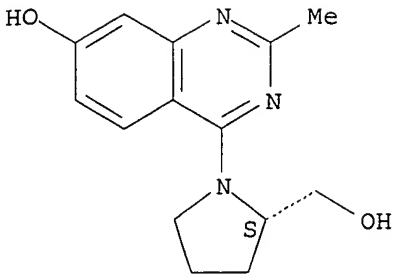
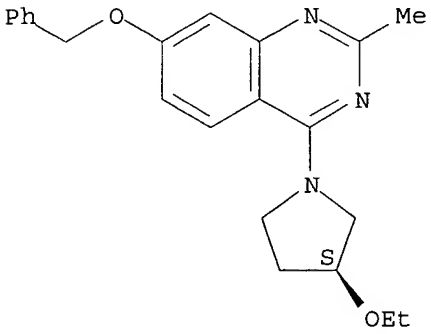
Absolute stereochemistry.



RN 646450-73-9 CAPLUS
CN Quinazoline, 4-[(3S)-3-ethoxy-1-pyrrolidinyl]-2-methyl-7-(phenylmethoxy)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 646450-74-0 CAPLUS
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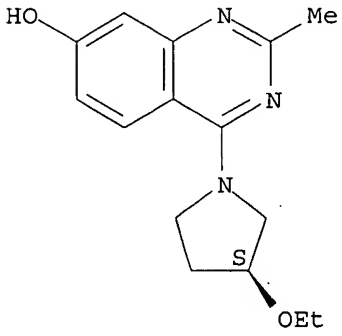
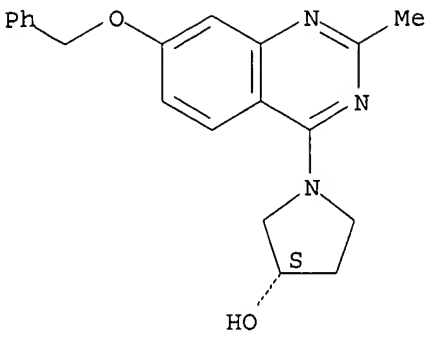
Absolute stereochemistry.



RN 646450-76-2 CAPLUS
CN 3-Pyrrolidinol, 1-[2-methyl-7-(phenylmethoxy)-4-quinazolinyl]-, (3S)- (9CI) (CA INDEX NAME)

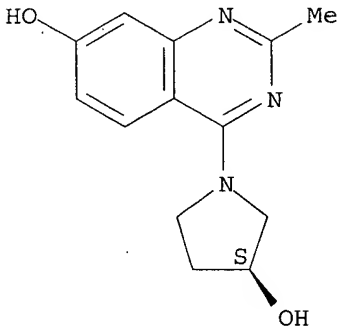
Absolute stereochemistry.

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86



RN 646450-77-3 CAPLUS
CN 7-Quinazolinol, 4-[(3S)-3-hydroxy-1-pyrrolidinyl]-2-methyl- (9CI) (CA INDEX NAME)

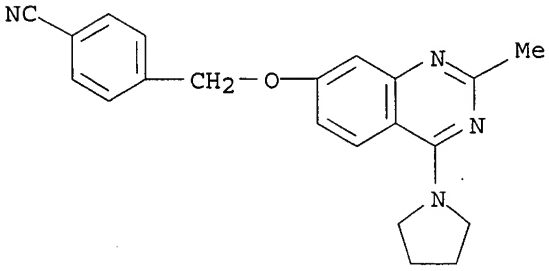
Absolute stereochemistry.



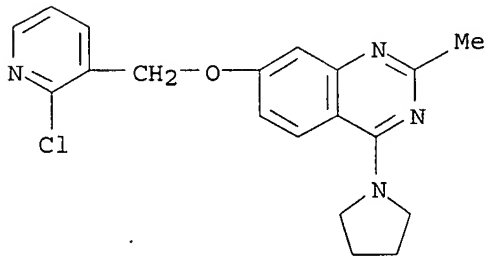
IT **646450-56-8P**, 4-[[[2-Methyl-4-(pyrrolidin-1-yl)quinazolin-7-yl]oxy]methyl]benzonitrile **646450-58-0P**, 7-(2-Chloropyridin-3-ylmethoxy)-2-methyl-4-pyrrolidin-1-ylquinazoline **646450-61-5P**, 2-[[[2-Methyl-4-(pyrrolidin-1-yl)quinazolin-7-yl]oxy]methyl]benzonitrile **646450-62-6P**, 7-(2-Fluoropyridin-3-ylmethoxy)-2-methyl-4-pyrrolidin-1-ylquinazoline **646450-63-7P**, 5-[[[2-Methyl-4-(pyrrolidin-1-yl)quinazolin-7-yl]oxy]methyl]pyridine-2-carbonitrile **646450-64-8P**, 7-Cyclopropylmethoxy-2-methyl-4-pyrrolidin-1-ylquinazoline hydrochloride **646450-65-9P**, 4-[[2-Methyl-4-(pyrrolidin-1-yl)quinazolin-7-yl]oxy]benzonitrile **646450-68-2P**, (S)-4-[[[4-(2-Hydroxymethylpyrrolidin-1-yl)-2-methylquinazolin-7-yl]oxy]methyl]benzonitrile **646450-69-3P**, (S)-[1-[7-(2-Chloropyridin-3-ylmethoxy)-2-methylquinazolin-4-yl]pyrrolidin-2-yl]methanol **646450-70-6P**, (S)-[1-[7-(2-Fluoropyridin-3-ylmethoxy)-2-methylquinazolin-4-yl]pyrrolidin-2-yl]methanol **646450-71-7P**, (S)-5-[[[4-(2-Hydroxymethylpyrrolidin-1-yl)-2-methylquinazolin-7-yl]oxy]methyl]pyridine-2-carbonitrile **646450-72-8P**, (S)-[1-[7-(Cyclopropylmethoxy)-2-methylquinazolin-4-yl]pyrrolidin-2-yl]methanol **646450-75-1P**, (S)-4-[[[4-(3-Ethoxypyrrolidin-1-yl)-2-methylquinazolin-7-yl]oxy]methyl]benzonitrile **646450-79-5P**, (Cyclopropylmethyl)[2-methyl-4-(pyrrolidin-1-yl)quinazolin-7-yl]amine **646450-80-8P**, (Isobutyl)[2-methyl-4-(pyrrolidin-1-yl)quinazolin-7-yl]amine **646450-81-9P**, (2,2-Dimethylpropyl)[2-methyl-4-(pyrrolidin-1-yl)quinazolin-7-yl]amine **646450-82-0P**, (2-Chlorobenzyl)[2-methyl-4-(pyrrolidin-1-

yl)quinazolin-7-yl]amine **646450-83-1P**, (2-Methylbenzyl)[2-methyl-4-(pyrrolidin-1-yl)quinazolin-7-yl]amine **646450-84-2P**, 4-[[2-Methyl-4-(pyrrolidin-1-yl)quinazolin-7-yl]amino]benzonitrile **646450-85-3P**, (4-Fluorophenyl)[2-methyl-4-(pyrrolidin-1-yl)quinazolin-7-yl]amine **646450-86-4P**, [2-Methyl-4-(pyrrolidin-1-yl)quinazolin-7-yl](pyridin-3-yl)amine **646450-87-5P**, Furan-2-carboxylic acid N-[2-methyl-4-(pyrrolidin-1-yl)quinazolin-7-yl]amide **646450-88-6P**, (S)-[4-(3-Ethoxypyrrolidin-1-yl)-2-methylquinazolin-7-yl](pyridin-3-yl)amine **646450-89-7P**, (S)-[4-(3-Ethoxypyrrolidin-1-yl)-2-methylquinazolin-7-yl](4-fluorophenyl)amine **646450-90-0P**, (S)-[4-(3-Methoxypyrrolidin-1-yl)-2-methylquinazolin-7-yl](pyridin-3-yl)amine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of quinazoline derivs. as NPY antagonists for treatment of obesity, etc.)

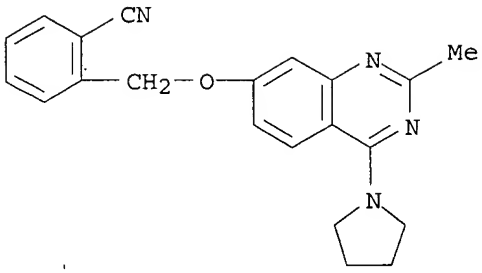
RN 646450-56-8 CAPLUS
CN Benzonitrile, 4-[[[2-methyl-4-(1-pyrrolidinyl)-7-quinazolinyl]oxy]methyl]- (9CI) (CA INDEX NAME)



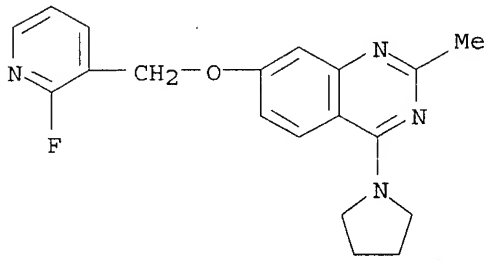
RN 646450-58-0 CAPLUS
CN Quinazoline, 7-[(2-chloro-3-pyridinyl)methoxy]-2-methyl-4-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



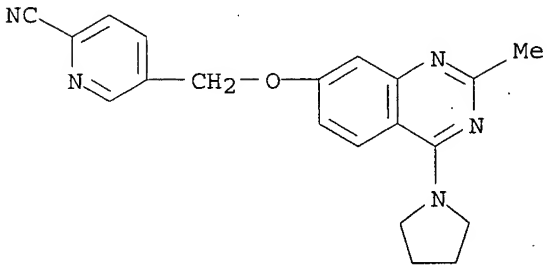
RN 646450-61-5 CAPLUS
CN Benzonitrile, 2-[[[2-methyl-4-(1-pyrrolidinyl)-7-quinazolinyl]oxy]methyl]- (9CI) (CA INDEX NAME)



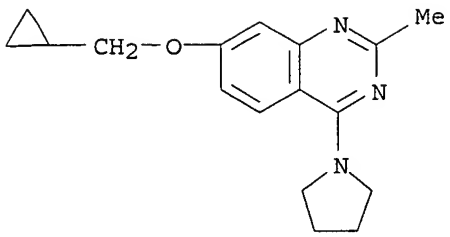
RN 646450-62-6 CAPLUS
CN Quinazoline, 7-[(2-fluoro-3-pyridinyl)methoxy]-2-methyl-4-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



RN 646450-63-7 CAPLUS
CN 2-Pyridinecarbonitrile, 5-[[[2-methyl-4-(1-pyrrolidinyl)-7-quinazolinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

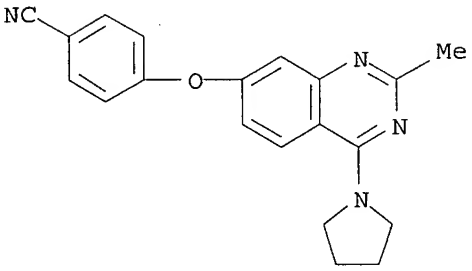


RN 646450-64-8 CAPLUS
CN Quinazoline, 7-(cyclopropylmethoxy)-2-methyl-4-(1-pyrrolidinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



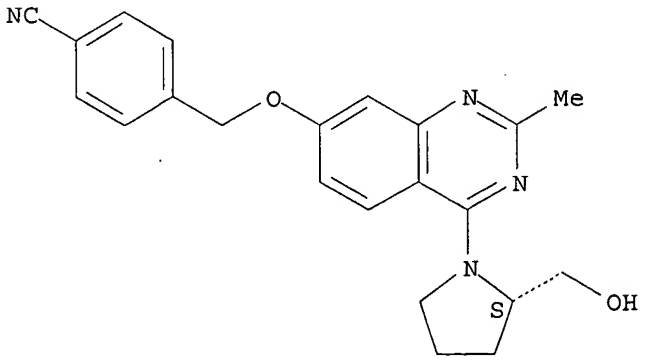
● HCl

RN 646450-65-9 CAPLUS
CN Benzonitrile, 4-[[2-methyl-4-(1-pyrrolidinyl)-7-quinazolinyl]oxy]- (9CI) (CA INDEX NAME)



RN 646450-68-2 CAPLUS
CN Benzonitrile, 4-[[[4-[(2S)-2-(hydroxymethyl)-1-pyrrolidinyl]-2-methyl-7-quinazolinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

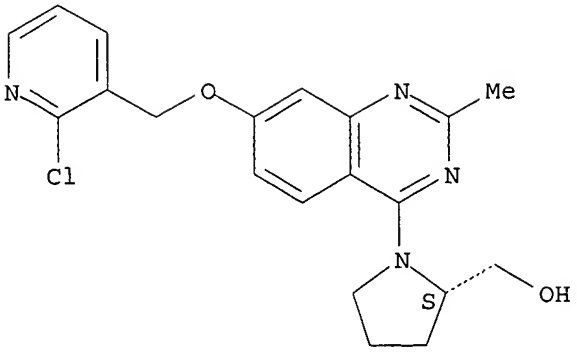
Absolute stereochemistry.



RN 646450-69-3 CAPLUS
CN 2-Pyrrolidinemethanol, 1-[7-[(2-chloro-3-pyridinyl)methoxy]-2-methyl-4-quinazolinyl]-, (2S)- (9CI) (CA INDEX NAME)

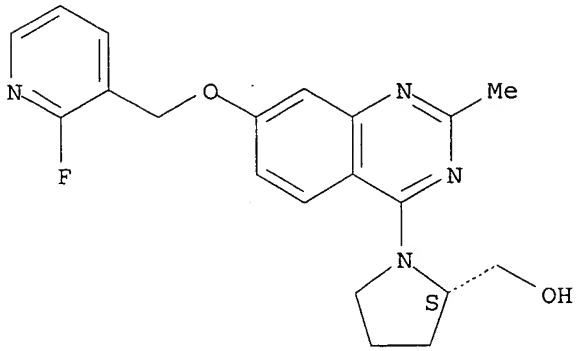
Absolute stereochemistry.

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86



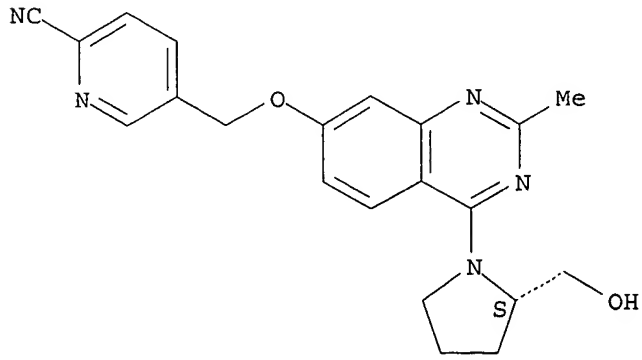
RN 646450-70-6 CAPLUS
CN 2-Pyrrolidinemethanol, 1-[7-[(2-fluoro-3-pyridinyl)methoxy]-2-methyl-4-quinazolinyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 646450-71-7 CAPLUS
CN 2-Pyridinecarbonitrile, 5-[[[4-[(2S)-2-(hydroxymethyl)-1-pyrrolidinyl]-2-methyl-7-quinazolinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

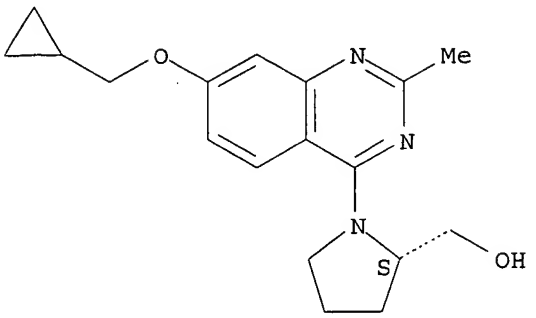
Absolute stereochemistry.



RN 646450-72-8 CAPLUS
CN 2-Pyrrolidinemethanol, 1-[7-(cyclopropylmethoxy)-2-methyl-4-quinazolinyl]-, (2S)- (9CI) (CA INDEX NAME)

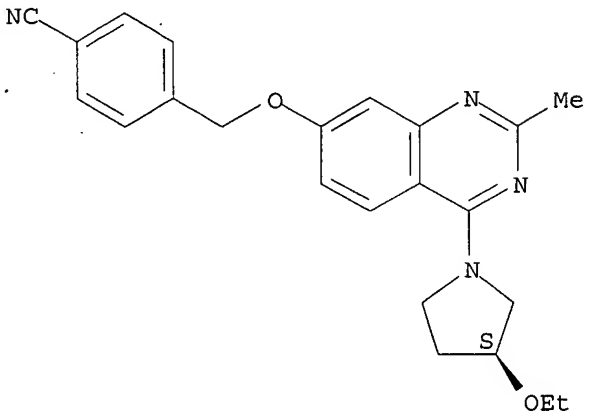
Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

Absolute stereochemistry.

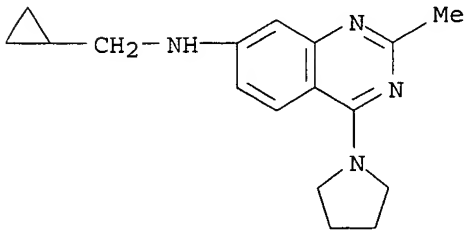


RN 646450-75-1 CAPLUS
CN Benzonitrile, 4-[[[4-[(3S)-3-ethoxy-1-pyrrolidinyl]-2-methyl-7-quinazolinyl]oxy]methyl]- (9CI) (CA INDEX NAME)

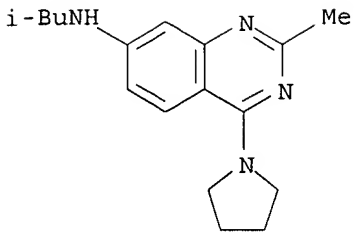
Absolute stereochemistry.



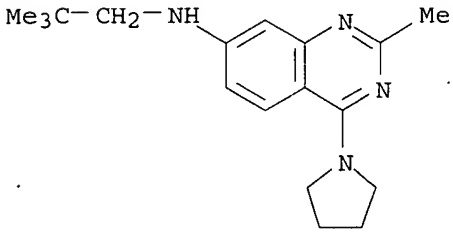
RN 646450-79-5 CAPLUS
CN 7-Quinazolinamine, N-(cyclopropylmethyl)-2-methyl-4-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



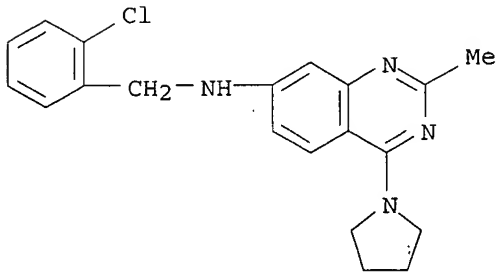
RN 646450-80-8 CAPLUS
CN 7-Quinazolinamine, 2-methyl-N-(2-methylpropyl)-4-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



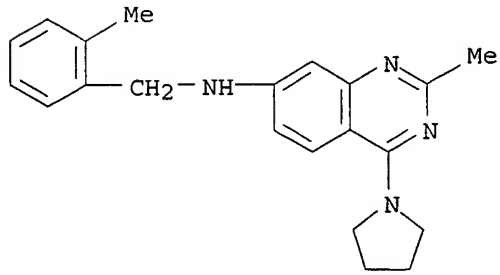
RN 646450-81-9 CAPLUS
CN 7-Quinazolinamine, N-(2,2-dimethylpropyl)-2-methyl-4-(1-pyrrolidinyl)-
(9CI) (CA INDEX NAME)



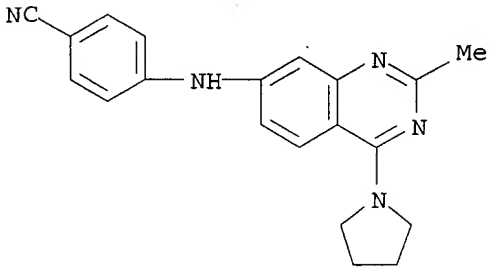
RN 646450-82-0 CAPLUS
CN 7-Quinazolinamine, N-[(2-chlorophenyl)methyl]-2-methyl-4-(1-pyrrolidinyl)-
(9CI) (CA INDEX NAME)



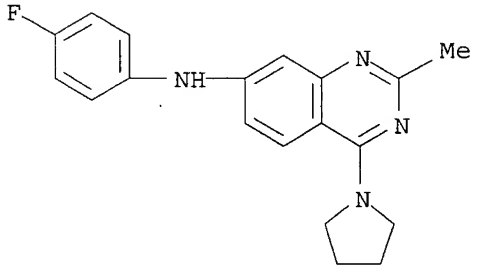
RN 646450-83-1 CAPLUS
CN 7-Quinazolinamine, 2-methyl-N-[(2-methylphenyl)methyl]-4-(1-pyrrolidinyl)-
(9CI) (CA INDEX NAME)



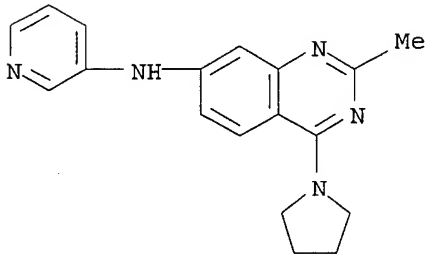
RN 646450-84-2 CAPLUS
CN Benzonitrile, 4-[[2-methyl-4-(1-pyrrolidinyl)-7-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



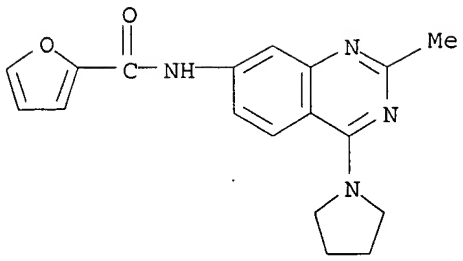
RN 646450-85-3 CAPLUS
CN 7-Quinazolinamine, N-(4-fluorophenyl)-2-methyl-4-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



RN 646450-86-4 CAPLUS
CN 7-Quinazolinamine, 2-methyl-N-3-pyridinyl-4-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)

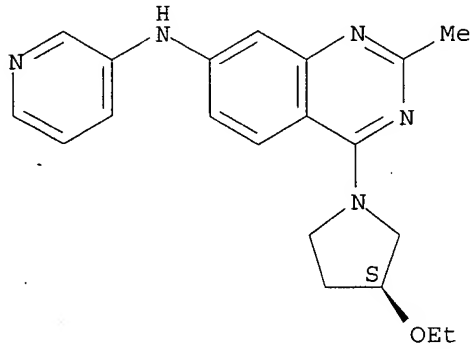


RN 646450-87-5 CAPLUS
CN 2-Furancarboxamide, N-[2-methyl-4-(1-pyrrolidinyl)-7-quinazolinyl]- (9CI) (CA INDEX NAME)



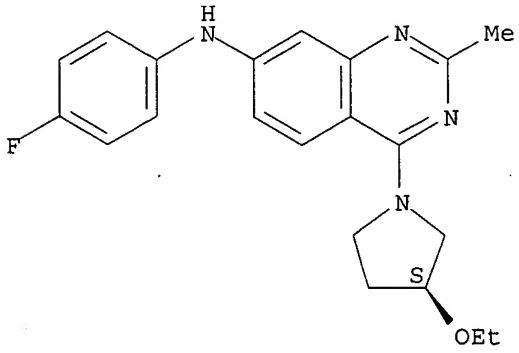
RN 646450-88-6 CAPLUS
CN 7-Quinazolinamine, 4-[(3S)-3-ethoxy-1-pyrrolidinyl]-2-methyl-N-3-pyridinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



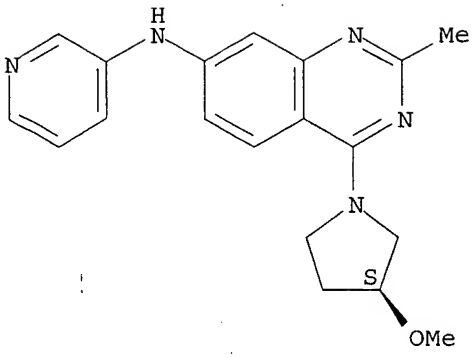
RN 646450-89-7 CAPLUS
CN 7-Quinazolinamine, 4-[(3S)-3-ethoxy-1-pyrrolidinyl]-N-(4-fluorophenyl)-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 646450-90-0 CAPLUS
CN 7-Quinazolinamine, 4-[(3S)-3-methoxy-1-pyrrolidinyl]-2-methyl-N-3-pyridinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:172597 CAPLUS
DOCUMENT NUMBER: 130:209716
TITLE: Preparation of 2-vinyl-4-aminoquinazoline derivatives as insulin secretion promoters and antidiabetics
INVENTOR(S): Ueno, Kimihisa; Nomoto, Yuji; Takasaki, Kotaro; Yoshida, Miho; Kusaka, Hideaki; Yano, Hiroshi; Nakanishi, Satoshi; Matsuda, Yuzuru; Uesaka, Noriaki; Suzuki, Chiharu
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan; et al.
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9909986	A1	19990304	WO 1998-JP3711		19980821
W: AU, BG, BR, CA, CN, CZ, HU, IL, JP, KR, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
AU 9887487	A1	19990316	AU 1998-87487		19980821
PRIORITY APPLN. INFO.:			JP 1997-225963	A	19970822
			WO 1998-JP3711	W	19980821

OTHER SOURCE(S): MARPAT 130:209716
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Claimed are insulin secretion promoters and remedies for diabetes which contain as the active ingredient 2-vinyl-4-aminoquinazoline derivs. represented by general formula (I) or pharmacol. acceptable salts thereof [wherein R1A and R1B are the same or different and each represents hydrogen, lower alkyl, lower alkoxy, halogeno, nitro, NR3R4 (wherein R3 and R4 are the same or different and each represents hydrogen or lower alkyl), etc.; or R1A may form together with R1B adjacent thereto O(CH2)nO

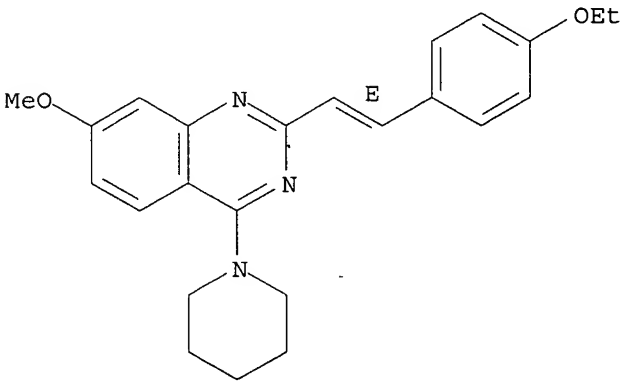
(wherein n is 1 or 2); Cy represents optionally substituted aryl; R2 represents hydrogen or optionally substituted lower alkyl; and A represents hydrogen or optionally substituted lower alkyl, optionally substituted cycloalkyl, etc.; or R2 and A may form together with the nitrogen atom adjacent thereto an optionally substituted heterocycle]. These compds. exhibited insulin secretion activity at high concentration of glucose (14.5 mM) but no substantial activity at low concentration of glucose (≤5 mM). For comparison, glubenclamide did exhibit substantial insulin-secretion activity at low concentration of glucose. Thus, 7-chloro-7-methoxy-2-[2-(E)-(2,4-dimethoxyphenyl)vinyl]quinazoline was condensed with N-methylphenethylamine to give the title compound (II). II in vitro showed insulin secretion activity of 3,413 ng/mL at 1 μM under 14.5 mM glucose and 86 ng/mL at 10 μM under 5 mM glucose in spleen β-cells (MIN6)as compared to that of 684 ng/mL at 0.1 μM under 14.5 mM glucose and 317 ng/mL at 0.1 μM under 5 mM glucose for glubenclamide.

IT **221008-87-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of vinylaminoquinazoline derivs. as insulin secretion promoters and antidiabetics)

RN 221008-87-3 CAPLUS

CN Quinazoline, 2-[(1E)-2-(4-ethoxyphenyl)ethenyl]-7-methoxy-4-(1-piperidinyl)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:490317 CAPLUS
DOCUMENT NUMBER: 117:90317
TITLE: Preparation of 2,4-diaminoquinazolines for enhancing antitumor activity
INVENTOR(S): Coe, Jotham Wadsworth; Fliri, Anton Franz; Kaneko, Takushi; Larson, Eric Robert
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

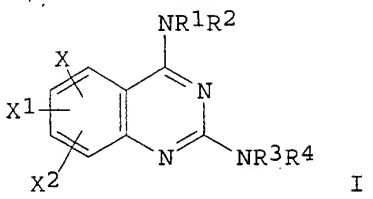
Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9207844	A1	19920514	WO 1991-US7254	19911010
W: AU, BR, CA, CS, DE, FI, HU, JP, KR, NO, PL, SU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2095213	AA	19920507	CA 1991-2095213	19911010
AU 9190592	A1	19920526	AU 1991-90592	19911010
AU 644035	B2	19931202		
EP 556310	A1	19930825	EP 1992-900750	19911010
EP 556310	B1	19950705		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05507290	T2	19931021	JP 1992-501815	19911010
HU 64533	A2	19940128	HU 1993-1314	19911010
BR 9107070	A	19940531	BR 1991-7070	19911010
ES 2074867	T3	19950916	ES 1992-900750	19911010
CN 1061411	A	19920527	CN 1991-108479	19911105
ZA 9108767	A	19930505	ZA 1991-8767	19911105
NO 9301635	A	19930505	NO 1993-1635	19930505
US 5444062	A	19950822	US 1993-50047	19930505
PRIORITY APPLN. INFO.:			US 1990-609986	A1 19901106
			WO 1991-US7254	A 19911010

OTHER SOURCE(S): MARPAT 117:90317

GI



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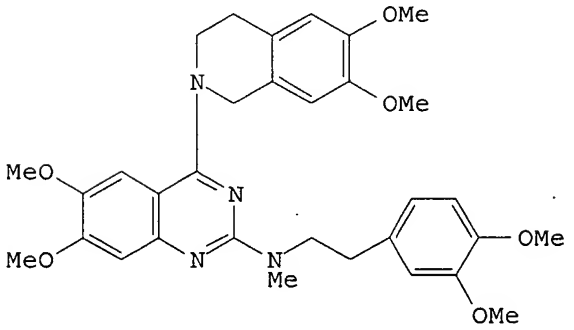


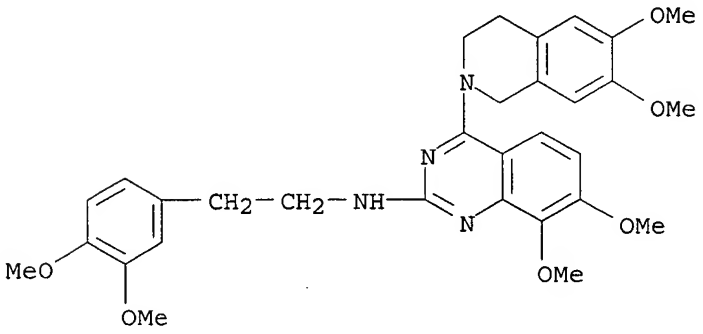
II

AB Title compds. [I; X, X1 = H, alkyl, alkoxy, Br, iodo, NO2, amino, Me2S+, aminomethyl, MeS, HOCH2, (substituted) benzoylamino, alkanoylamino, 4-methylpiperazino, morpholino, piperazino, pyrrolidino, etc.; X2 = H, alkyl, alkoxy; XX1 = ethylenedioxy, methylenedioxy; R1 = alkoxyalkyl, cycloalkyl, benzodioxan-2-ylmethyl; R2 = H, alkyl, PhCH2; R1R2 = (substituted) benzodiazepinyl, piperidino, decahydroisoquinol-2-yl, octahydroisoindol-2-yl, 1,2,3,4-tetrahydro-β-carbol-2-yl; R3 = cycloalkyl, benzodioxan-2-ylmethyl, (substituted) aralkyl, pyridylalkyl,

alkoxyalkyl, indolylalkyl, tetrahydronaphthyl, indenyl, naphthyl, etc.; R4 = H, alkyl; R3R4N = (substituted) tetrahydroisoquinolyl, piperidino, piperazino], were prepared as p-glycoprotein inhibitors to reverse multidrug resistance (no data). Thus, 2,4-dichloro-6,7-dimethoxyquinazoline, 1,2,3,4-tetrahydro-6,7-dimethoxyisoquinoline, and Et3N were stirred 16 h in dimethylacetamide to give 2-chloro-4-(1,2,3,4-tetrahydro-6,7-dimethoxyisoquinol-2-yl)-6,7-dimethoxyquinazoline. The latter was heated with N-methyl-3,4-dimethoxyphenethylamine in ethoxyethoxyethanol to give title compound II.

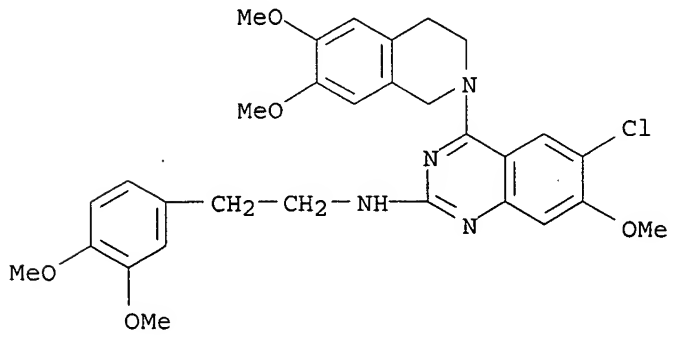
IT **142716-12-9P 142735-40-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as P-glycoprotein inhibitor)

RN 142716-12-9 CAPLUS
CN 2-Quinazolinamine, 4-(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)-N-[2-(3,4-dimethoxyphenyl)ethyl]-7,8-dimethoxy-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 142735-40-8 CAPLUS
CN 2-Quinazolinamine, 6-chloro-4-(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)-N-[2-(3,4-dimethoxyphenyl)ethyl]-7-methoxy- (9CI) (CA INDEX NAME)



L8 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1972:405511 CAPLUS
DOCUMENT NUMBER: 77:5511

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

TITLE: 2-Styryl-4-aminoquinazolines
INVENTOR(S): Breuer, Hermann; Schulze, Ernst
PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc.
SOURCE: Ger. Offen., 18 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2135172	A	19720120	DE 1971-2135172	19710714
US 3753981	A	19730821	US 1970-55252	19700715
CH 532056	A	19730215	CH 1971-532056	19710714
CA 971962	A1	19750729	CA 1971-118193	19710714
FR 2100916	A5	19720324	FR 1971-25952	19710715
FR 2100916	B1	19741018		
HU 163174	P	19730628	HU 1971-SU648	19710715
GB 1364294	A	19740821	GB 1971-33228	19710715

PRIORITY APPLN. INFO.: US 1970-55252 A 19700715

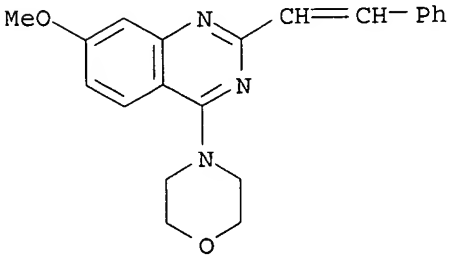
GI For diagram(s), see printed CA Issue.

AB The title compds. [I, R = NHCHMe(CH2)3NEt2, morpholino, or 4-methyl-1-piperazinyl; R1 = H, Cl, OMe, or NO2; R2 = H or Cl], useful as antiinflammatory agents, were prepared by treatment of 2-styryl-4(3H)-quinazolinones with POCl3 to give I (R = Cl) and reaction with amines. Thus, 28.3 g 6-chloro-2-styryl-4(3H)-quinazolinone was refluxed 4 hr with POCl3 in PhNMe2 and C6H6 to give I (R = Cl, R1 = 6-Cl, R2 = H). Similarly prepared were 8 I (R = Cl), e.g. (R1 and R2 given): 7-Cl, H (II); 6-OMe, Cl. Refluxing 8.4 g II 15 hr with H2NCHMe(CH2)3NEt2 in C6H6 gave 9.25 g I [R = NHCHMe(CH2)3NEt2, R1 = 7-Cl, R2 = H], from which the di-HCl salt was also prepared Similarly prepared were 14 addnl. I, e.g.. (R-R2 and salt given): morpholino, 7-Cl, Cl, -; 4-methyl-1-piperazinyl, 6-Cl, H, 1.5HCl.0.5H2O; NHCHMe(CH2)3NEt2, 7-OMe, H, 2HCl.2H2O.

IT **36945-47-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 36945-47-8 CAPLUS

CN Quinazoline, 7-methoxy-4-(4-morpholinyl)-2-(2-phenylethenyl)- (9CI) (CA INDEX NAME)



=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	25.10	187.93

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.92	-2.92

FILE 'REGISTRY' ENTERED AT 11:00:18 ON 29 NOV 2005

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 28 NOV 2005 HIGHEST RN 868827-82-1
DICTIONARY FILE UPDATES: 28 NOV 2005 HIGHEST RN 868827-82-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

```
=> e "4-(2-methyl-4-pyrrolidin-1-yl-quinazolin-7-yloxymethyl)-benzonitrile"/cn
E1            1     4-(2-METHYL-4-PYRIDYL)PIPERAZINE-2-CARBOXYLIC ACID TERT-BUTY
                    L ESTER/CN
E2            1     4-(2-METHYL-4-PYRIMIDINYL)-1-PIPERAZINESULFONAMIDE/CN
E3            0 --> 4-(2-METHYL-4-PYRROLIDIN-1-YL-QUINAZOLIN-7-YLOXYMETHYL)-BENZ
                    ONITRILE/CN
E4            1     4-(2-METHYL-4-QUINOLINYL)BENZOIC ACID/CN
E5            1     4-(2-METHYL-4-THIAZOLYL)PYRIDINE/CN
E6            1     4-(2-METHYL-5,6,7,8-TETRAHYDROQUINOLIN-7-YLMETHYL)-1,3-DIHYD
                    ROIMIDAZOLE-2-THIONE/CN
E7            1     4-(2-METHYL-5-((2-THIOXO-2,3-DIHYDRO-1H-IMIDAZOL-4-YL)METHYL
                    )CYCLOPENT-1-ENYL)BENZONITRILE/CN
E8            1     4-(2-METHYL-5-((PIPERIDIN-1-YL)SULFONYL)PHENYL)-4-OXOBUTYRAL
                    DEHYDE/CN
E9            1     4-(2-METHYL-5-(METHOXYCARBONYL)ANILINO)-2-(3-PYRIDINYL)-6-(T
                    RIFLUOROMETHYL)PYRIMIDINE/CN
E10           1     4-(2-METHYL-5-(METHYLSULFONYL)-1H-INDOL-3-YL)-8-(TRIFLUOROME
                    THYL)QUINOLINE/CN
E11           1     4-(2-METHYL-5-(TRIFLUOROMETHYL)-1H-INDOL-3-YL)-8-(TRIFLUOROM
```

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

```
                    ETHYL)QUINOLINE/CN
E12           1     4-(2-METHYL-5-(TRIFLUOROMETHYL)ANILINO)-2-(3-PYRIDINYL)-6-(T
                    RIFLUOROMETHYL)PYRIMIDINE/CN

=> e "7-(2-chloro-pyridin-3-ylmethoxy)-2-methyl-4-pyrrolidin-1-yl-quinazoline"/cn
E1            1     7-(2-CHLORO-6-METHYLBENZENESULFONYL)-1-PIPERAZIN-1-YLISOQUIN
                    OLINE/CN
E2            1     7-(2-CHLORO-6-METHYLBENZENESULFONYL)-1-PIPERAZIN-1-YLISOQUIN
                    OLINE MONOHYDROCHLORIDE/CN
E3            0 --> 7-(2-CHLORO-PYRIDIN-3-YLMETHOXY)-2-METHYL-4-PYRROLIDIN-1-YL-
                    QUINAZOLINE/CN
E4            1     7-(2-CHLOROACETYL)-1,3,4,5-TETRAHYDROBENZO(B)AZEPIN-2-ONE/CN
E5            1     7-(2-CHLOROACETYL)-5,5-DIMETHYL-1,3,4,5-TETRAHYDROBENZO(B)AZ
                    EPIN-2-ONE/CN
E6            1     7-(2-CHLOROACETYL)AMINO-9A-METHOXYMITOSAN/CN
E7            1     7-(2-CHLOROBENZOYL)-2,3,4,5-TETRAHYDRO-1-BENZOXEPIN/CN
E8            1     7-(2-CHLOROBENZYL)-2-(TRIFLUOROMETHYL)-2H-CHROMENE-3-CARBOXY
                    LIC ACID/CN
E9            1     7-(2-CHLOROBENZYLOXY)-1-(2-METHYLPROPYL)-2-PROPYL-1H-IMIDAZO
                    (4,5-C)QUINOLIN-4-AMINE/CN
E10           1     7-(2-CHLOROBENZYLOXY)-2-(ETHOXYMETHYL)-1-(2-METHYLPROPYL)-1H
                    -IMIDAZO(4,5-C)QUINOLIN-4-AMINE/CN
E11           1     7-(2-CHLOROBENZYLOXY)-2-(MORPHOLIN-4-YL)-CHROMEN-4-ONE/CN
E12           1     7-(2-CHLOROETHANOYL)-1H-PYRIDO(2,3-B)(1,4)THIAZIN-2-ONE/CN

=> s methyl(l)pyrrolidin?(l)quinazolin?(l)oxymethyl(l)benzonitrile
      15813450 METHYL
            95 METHYLS
      15813450 METHYL
                 (METHYL OR METHYLS)
        528275 PYRROLIDIN?
        292151 QUINAZOLIN?
        195561 OXYMETHYL
         71835 BENZONITRILE
L9           0 METHYL(L)PYRROLIDIN?(L)QUINAZOLIN?(L)OXYMETHYL(L)BENZONITRILE

=> s methyl(l)pyrrolidin?(l)quinazolin?(l)yloxymethyl(l)benzonitrile
      15813450 METHYL
            95 METHYLS
      15813450 METHYL
                 (METHYL OR METHYLS)
        528275 PYRROLIDIN?
        292151 QUINAZOLIN?
          3048 YLOXYMETHYL
         71835 BENZONITRILE
L10          0 METHYL(L)PYRROLIDIN?(L)QUINAZOLIN?(L)YLOXYMETHYL(L)BENZONITRILE

=> s chloro(l)pyridin?(l)ylmethoxy(l)methyl(l)pyrrolidin?(l)quinazoline?
       4116117 CHLORO
            46 CHLOROS
       4116117 CHLORO
                 (CHLORO OR CHLOROS)
       1842252 PYRIDIN?
         84448 YLMETHOXY
      15813450 METHYL
            95 METHYLS
      15813450 METHYL
                 (METHYL OR METHYLS)
        528275 PYRROLIDIN?
         68401 QUINAZOLINE?
```

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```
L11           1 CHLORO(L)PYRIDIN?(L)YLMETHOXY(L)METHYL(L)PYRROLIDIN?(L)QUINAZOLI
                NE?

s fluoro(l)pyridin?(l)ylmethoxy(l)methyl(l)pyrrolidin?(l)quinazoline?

       2894185 FLUORO
            15 FLUOROS
       2894185 FLUORO
                 (FLUORO OR FLUOROS)
       1842252 PYRIDIN?
         84448 YLMETHOXY
      15813450 METHYL
            95 METHYLS
      15813450 METHYL
                 (METHYL OR METHYLS)
        528275 PYRROLIDIN?
         68401 QUINAZOLINE?
L12           1 FLUORO(L)PYRIDIN?(L)YLMETHOXY(L)METHYL(L)PYRROLIDIN?(L)QUINAZOLI
                NE?

=> s chloro(l)pyridin?(l)ylmethoxy(l)methyl(l)quinazolin?(l)pyrrolidin(l)methanol
       4116117 CHLORO
            46 CHLOROS
       4116117 CHLORO
                 (CHLORO OR CHLOROS)
       1842252 PYRIDIN?
         84448 YLMETHOXY
      15813450 METHYL
            95 METHYLS
      15813450 METHYL
                 (METHYL OR METHYLS)
        292151 QUINAZOLIN?
        336910 PYRROLIDIN
        290558 METHANOL
L13           1 CHLORO(L)PYRIDIN?(L)YLMETHOXY(L)METHYL(L)QUINAZOLIN?(L)PYRROLIDI
                N(L)METHANOL

=> s ethoxy(l)pyrrolidin?(l)methyl(l)quinazolin?(l)yloxymethyl(l)benzonitrile
       1348039 ETHOXY
        528275 PYRROLIDIN?
      15813450 METHYL
            95 METHYLS
      15813450 METHYL
                 (METHYL OR METHYLS)
        292151 QUINAZOLIN?
          3048 YLOXYMETHYL
         71835 BENZONITRILE
L14           0 ETHOXY(L)PYRROLIDIN?(L)METHYL(L)QUINAZOLIN?(L)YLOXYMETHYL(L)BENZ
                ONITRILE

=> s isobutyl(l)methyl(l)pyrrolidin?(l)quinazolin?(l)amine
         26119 ISOBUTYL
             2 ISOBUTYLS
         26119 ISOBUTYL
                 (ISOBUTYL OR ISOBUTYLS)
      15813450 METHYL
            95 METHYLS
      15813450 METHYL
                 (METHYL OR METHYLS)
        528275 PYRROLIDIN?
```

```
        292151 QUINAZOLIN?
       1523418 AMINE
          1185 AMINES
       1523418 AMINE
                 (AMINE OR AMINES)
L15          1 ISOBUTYL(L)METHYL(L)PYRROLIDIN?(L)QUINAZOLIN?(L)AMINE

=> s methyl(l)pyrrolidin?(l)quinazolin?(l)pyridin?(l)amine?
      15813450 METHYL
            95 METHYLS
      15813450 METHYL
                 (METHYL OR METHYLS)
        528275 PYRROLIDIN?
        292151 QUINAZOLIN?
       1842252 PYRIDIN?
       1523429 AMINE?
L16          41 METHYL(L)PYRROLIDIN?(L)QUINAZOLIN?(L)PYRIDIN?(L)AMINE?

=> s furan(l)carboxylic acid(l)methyl(l)pyrrolidin?(l)quinazolin?(l)amide
        896047 FURAN
             3 FURANS
        896047 FURAN
                 (FURAN OR FURANS)
       1871822 CARBOXYLIC
       7387839 ACID
          8814 ACIDS
       7394423 ACID
                 (ACID OR ACIDS)
       1861934 CARBOXYLIC ACID
                 (CARBOXYLIC(W)ACID)
      15813450 METHYL
            95 METHYLS
      15813450 METHYL
                 (METHYL OR METHYLS)
        528275 PYRROLIDIN?
        292151 QUINAZOLIN?
       3768134 AMIDE
          1053 AMIDES
       3768134 AMIDE
                 (AMIDE OR AMIDES)
L17          1 FURAN(L)CARBOXYLIC ACID(L)METHYL(L)PYRROLIDIN?(L)QUINAZOLIN?(L)A
               MIDE

=> s ethoxy(l)pyrrolidin?(l)methyl(l)quinazolin?(l)pyridin?(l)amine
       1348039 ETHOXY
        528275 PYRROLIDIN?
      15813450 METHYL
            95 METHYLS
      15813450 METHYL
                 (METHYL OR METHYLS)
        292151 QUINAZOLIN?
       1842252 PYRIDIN?
       1523418 AMINE
          1185 AMINES
       1523418 AMINE
                 (AMINE OR AMINES)
L18          9 ETHOXY(L)PYRROLIDIN?(L)METHYL(L)QUINAZOLIN?(L)PYRIDIN?(L)AMINE

=> s methoxy(l)pyrrolidin?(l)methyl(l)quinazolin?(l)pyridin?(l)amine
       4233458 METHOXY
```

```
        528275 PYRROLIDIN?
      15813450 METHYL
            95 METHYLS
      15813450 METHYL
                 (METHYL OR METHYLS)
        292151 QUINAZOLIN?
       1842252 PYRIDIN?
       1523418 AMINE
          1185 AMINES
       1523418 AMINE
                 (AMINE OR AMINES)
L19          14 METHOXY(L)PYRROLIDIN?(L)METHYL(L)QUINAZOLIN?(L)PYRIDIN?(L)AMINE

=> fil medl,biosis,embase,caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   299.13     487.06

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -2.92

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=> s methoxy(l)pyrrolidin?(l)methyl(l)quinazolin?(l)pyridin?(l)amine or l19
L20           1 FILE MEDLINE
L21           0 FILE BIOSIS
L22           1 FILE EMBASE
L23           8 FILE CAPLUS

TOTAL FOR ALL FILES
L24          10 METHOXY(L) PYRROLIDIN?(L) METHYL(L) QUINAZOLIN?(L) PYRIDIN?(L)
                AMINE OR L19

=> s ethoxy(l)pyrrolidin?(l)methyl(l)quinazolin?(l)pyridin?(l)amine or l18
L25           0 FILE MEDLINE
L26           0 FILE BIOSIS
L27           0 FILE EMBASE
L28           6 FILE CAPLUS

TOTAL FOR ALL FILES
L29           6 ETHOXY(L) PYRROLIDIN?(L) METHYL(L) QUINAZOLIN?(L) PYRIDIN?(L)
                AMINE OR L18

=> s furan(l)carboxylic acid(l)methyl(l)pyrrolidin?(l)quinazolin?(l)amide or l17
L30           0 FILE MEDLINE
L31           0 FILE BIOSIS
L32           0 FILE EMBASE
L33           1 FILE CAPLUS
```

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

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TOTAL FOR ALL FILES
L34           1 FURAN(L) CARBOXYLIC ACID(L) METHYL(L) PYRROLIDIN?(L) QUINAZOLIN?
                (L) AMIDE OR L17

=> s methyl(l)pyrrolidin?(l)quinazolin?(l)pyridin?(l)amine? or l16
L35           1 FILE MEDLINE
L36           0 FILE BIOSIS
L37           1 FILE EMBASE
L38          14 FILE CAPLUS

TOTAL FOR ALL FILES
L39          16 METHYL(L) PYRROLIDIN?(L) QUINAZOLIN?(L) PYRIDIN?(L) AMINE? OR
                L16

=> s isobutyl(l)methyl(l)pyrrolidin?(l)quinazolin?(l)amine or l15
L40           0 FILE MEDLINE
L41           0 FILE BIOSIS
L42           0 FILE EMBASE
L43           1 FILE CAPLUS

TOTAL FOR ALL FILES
L44           1 ISOBUTYL(L) METHYL(L) PYRROLIDIN?(L) QUINAZOLIN?(L) AMINE OR L15

=> s ethoxy(l)pyrrolidin?(l)methyl(l)quinazolin?(l)yloxymethyl(l)benzonitrile or l14
L45           0 FILE MEDLINE
L46           0 FILE BIOSIS
L47           0 FILE EMBASE
L48           0 FILE CAPLUS

TOTAL FOR ALL FILES
L49           0 ETHOXY(L) PYRROLIDIN?(L) METHYL(L) QUINAZOLIN?(L) YLOXYMETHYL(L)
                 BENZONITRILE OR L14

=> s chloro(l)pyridin?(l)ylmethoxy(l)methyl(l)quinazolin?(l)pyrrolidin(l)methanol
or l13
L50           0 FILE MEDLINE
L51           0 FILE BIOSIS
L52           0 FILE EMBASE
L53           1 FILE CAPLUS

TOTAL FOR ALL FILES
L54           1 CHLORO(L) PYRIDIN?(L) YLMETHOXY(L) METHYL(L) QUINAZOLIN?(L)
                PYRROLIDIN(L) METHANOL OR L13

=> s fluoro(l)pyridin?(l)ylmethoxy(l)methyl(l)pyrrolidin?(l)quinazoline? or l12
L55           0 FILE MEDLINE
L56           0 FILE BIOSIS
L57           0 FILE EMBASE
L58           1 FILE CAPLUS

TOTAL FOR ALL FILES
L59           1 FLUORO(L) PYRIDIN?(L) YLMETHOXY(L) METHYL(L) PYRROLIDIN?(L)
                QUINAZOLINE? OR L12

=> s chloro(l)pyridin?(l)ylmethoxy(l)methyl(l)pyrrolidin?(l)quinazoline? or l11
L60           0 FILE MEDLINE
L61           0 FILE BIOSIS
L62           0 FILE EMBASE
L63           1 FILE CAPLUS
```

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

```
TOTAL FOR ALL FILES
L64          1 CHLORO(L) PYRIDIN?(L) YLMETHOXY(L) METHYL(L) PYRROLIDIN?(L)
               QUINAZOLINE? OR L11

=> s l24 or l29 or l34 or l39 or l44 or l54 or l59 or l64
L65          1 FILE MEDLINE
L66          0 FILE BIOSIS
L67          1 FILE EMBASE
L68         14 FILE CAPLUS

TOTAL FOR ALL FILES
L69         16 L24 OR L29 OR L34 OR L39 OR L44 OR L54 OR L59 OR L64

=> s l69 not l8
L70          1 FILE MEDLINE
L71          0 FILE BIOSIS
L72          1 FILE EMBASE
L73         13 FILE CAPLUS

TOTAL FOR ALL FILES
L74         15 L69 NOT L8

=> dup rem l74
PROCESSING COMPLETED FOR L74
L75          14 DUP REM L74 (1 DUPLICATE REMOVED)

=> d 1-14 ibib abs hitstr

L75  ANSWER 1 OF 14  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:1021616  CAPLUS
DOCUMENT NUMBER:          143:326381
TITLE:                    Preparation of arylalkylamino-substituted quinazolines
                          as type VR1 capsaicin receptor modulators
INVENTOR(S):              Bakthavatchalam, Rajagopal; Chenard, Bertrand L.;
                          Peterson, John M.; Steenstra, Cheryl K.
PATENT ASSIGNEE(S):       Neurogen Corporation, USA
SOURCE:                   PCT Int. Appl., 133 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND  DATE        APPLICATION NO.        DATE
     ---------------      ----  --------    --------------------   --------
     WO 2005087227         A1   20050922    WO 2005-US6697         20050301
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM,
             SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
             RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
             MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                    US 2004-550216P     P  20040304
GI

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86
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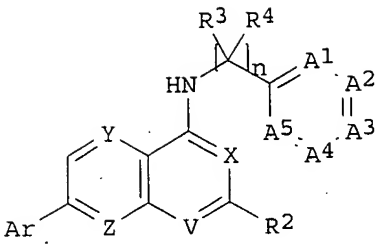

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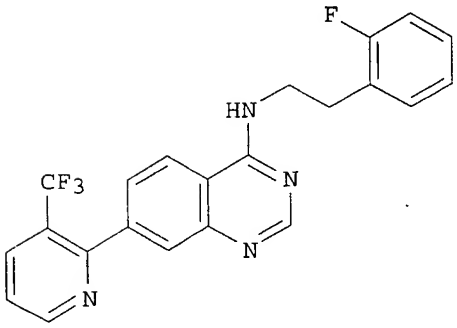


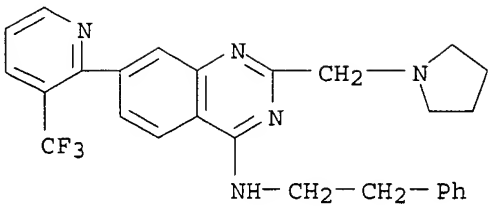
II

AB The title compds. I [V, X, Y and Z = N, CR1, such that at least one of V and X = N; R1 = H, halo, OH, etc.; R2 = halo, NO2, CN, etc.; n = 1-3; R3 = H, CN, alkyl, etc.; R4 = H, CN, alkyl; or R3 together with R4 forms an oxo group; or CR3R4 forms a 3-7 membered carbocycle or heterocycle; Ar = (un)substituted 5-10 membered carbocycle or heterocycle; A1 = N, CRa, or A1 is taken together with a R3 group to form an optionally substituted fused 5-7 membered carbocycle or heterocycle; A2-A5 = N, CRa; Ra = H, OH, halo, etc.] that are ligands that may be used to modulate specific receptor activity in vivo or in vitro, and are particularly useful in the treatment of conditions associated with pathol. receptor activation in humans, domesticated companion animals and livestock animals, were prepared Thus, reacting 4-chloro-7-(3-trifluoromethylpyridin-2-yl)quinazoline with 2-fluorophenethylamine afforded the quinazoline II. The compds. I were tested in various tests for evaluating the VR1 modulator activity (data given). Pharmaceutical compns. and methods for using the compds. I to treat condition responsive to capsaicin receptor modulation are provided, as are methods for using such ligands for receptor localization studies.

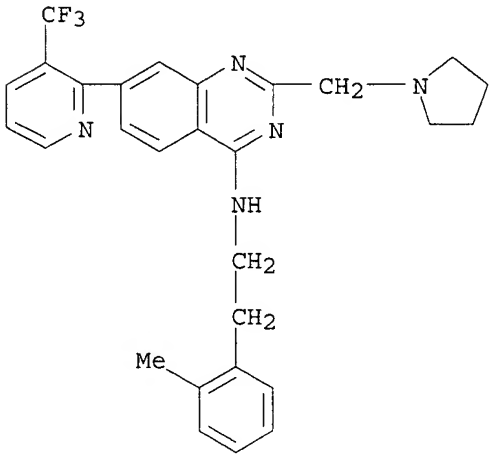
IT **865158-45-8P 865158-46-9P 865158-47-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of arylalkylamino-substituted quinazolines as type VR1 capsaicin receptor modulators)

RN 865158-45-8 CAPLUS

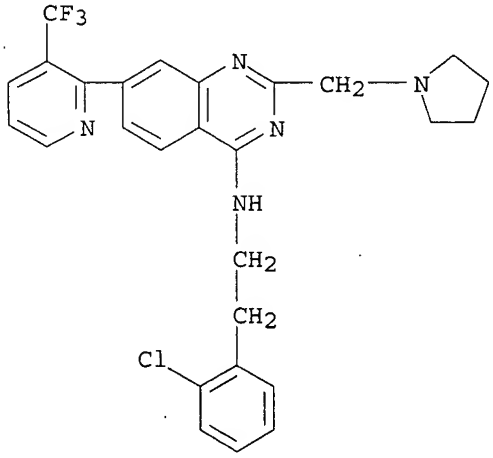
CN 4-Quinazolinamine, N-(2-phenylethyl)-2-(1-pyrrolidinylmethyl)-7-[3-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



RN 865158-46-9 CAPLUS
CN 4-Quinazolinamine, N-[2-(2-methylphenyl)ethyl]-2-(1-pyrrolidinylmethyl)-7-[3-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



RN 865158-47-0 CAPLUS
CN 4-Quinazolinamine, N-[2-(2-chlorophenyl)ethyl]-2-(1-pyrrolidinylmethyl)-7-[3-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

ACCESSION NUMBER: 2005:260055 CAPLUS
DOCUMENT NUMBER: 142:336380
TITLE: Preparation of quinazoline derivatives as EGFR tyrosine kinase inhibitors
INVENTOR(S): Bradbury, Robert Hugh; Hennequin, Laurent Francois Andre; Kettle, Jason Grant
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 203 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005026152	A1	20050324	WO 2004-GB3936	20040914

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2003-21648 A 20030916
OTHER SOURCE(S): MARPAT 142:336380
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = H, OH, alkoxy, etc.; Y = H, halo, alkenyl, etc; m = 0-4; R2 independently = halo, alkyl, alkynyl, etc.; X1 = C(R3)2; X2 = bond O, S, SO2, etc.; Q2 = (un)substituted-aryl, -heteroaryl; R3 = H, alkyl; Q1 = 4-, 5-, 6-, or 7-membered (un)saturated nitrogen heterocycle containing optionally 1 or 2 addnl. heteroatoms selected from O, S, and N, and which ring is linked to X1 via ring carbon; X3 = -(CR4R5)p-(Q3)n-(CR6R7)q-; n = 0-1; p = 0-4; q = 0-4; R4, R5, R6, R7 independently = H, alkyl; Q3 = cycloalkylene, cycloalkenylene; Z = OH, amino, alkanesulfonylamino, etc.;] and their pharmaceutically acceptable salts, are prepared and disclosed as useful for the treatment of certain cancers. Thus, e.g., II was prepared by amination of 4-chloro-5-fluoroquinazoline (preparation given) with 3-chloro-4-(2-pyridylmethoxy)aniline followed by substitution with R-prolinol and carbonylation with glycolic acid. The activity of I was evaluated in different inhibition assays directed at inhibiting phosphorylation, cell proliferation, and in vivo tumor growth and revealed that all compds. of the invention possessed IC50 values of 0.001-5 μM or activity in the range of 1-200 mg/kg/day. I as tyrosine kinase inhibitors should prove useful in the treatment of diseases such as certain cancers mediated by erbB receptor tyrosine kinases, particularly EGFR tyrosine kinase.

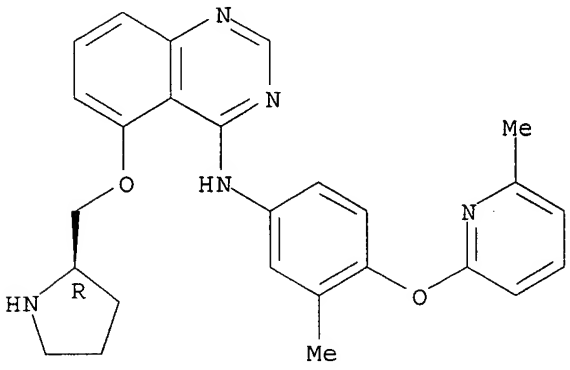
IT **848482-46-2P 848482-48-4P 848482-80-4P**
848482-84-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

(Reactant or reagent)
(preparation of quinazoline derivs. as inhibitors of EGFR tyrosine kinase)

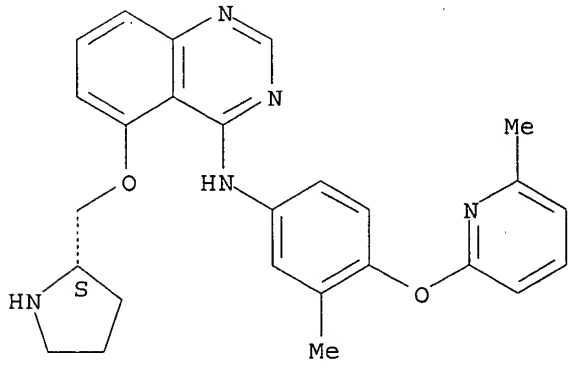
RN 848482-46-2 CAPLUS
CN 4-Quinazolinamine, N-[3-methyl-4-[(6-methyl-2-pyridinyl)oxy]phenyl]-5-[(2R)-2-pyrrolidinylmethoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



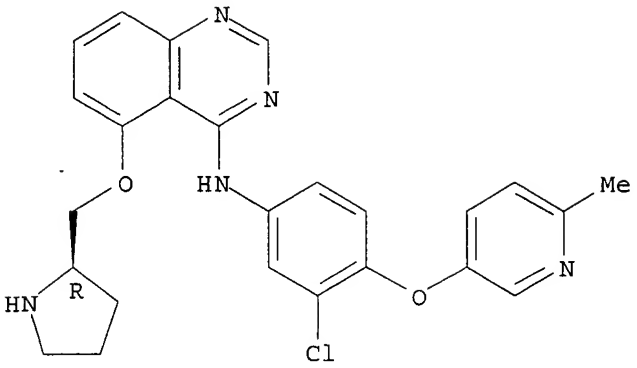
RN 848482-48-4 CAPLUS
CN 4-Quinazolinamine, N-[3-methyl-4-[(6-methyl-2-pyridinyl)oxy]phenyl]-5-[(2S)-2-pyrrolidinylmethoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



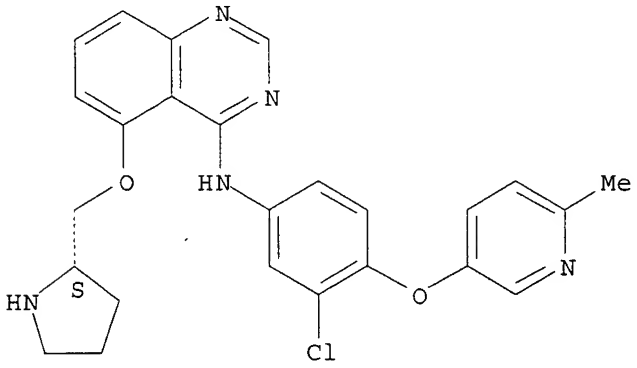
RN 848482-80-4 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(6-methyl-3-pyridinyl)oxy]phenyl]-5-[(2R)-2-pyrrolidinylmethoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 848482-84-8 CAPLUS
CN 4-Quinazolinamine, N-[3-chloro-4-[(6-methyl-3-pyridinyl)oxy]phenyl]-5-[(2S)-2-pyrrolidinylmethoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:411065 CAPLUS
DOCUMENT NUMBER: 142:441833
TITLE: Selective erbb2 inhibitor/anti-erbb antibody combinations in the treatment of cancer
INVENTOR(S): Connell, Richard D.; Denis, Louis J.; Jani, Jitesh P.
PATENT ASSIGNEE(S): Pfizer Inc, USA
SOURCE: U.S. Pat. Appl. Publ., 46 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005101618	A1	20050512	US 2004-982996	20041104
WO 2005044302	A1	20050519	WO 2004-IB3551	20041027

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-517636P P 20031106
US 2004-549600P P 20040303

OTHER SOURCE(S): MARPAT 142:441833

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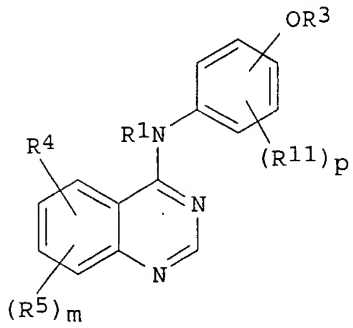


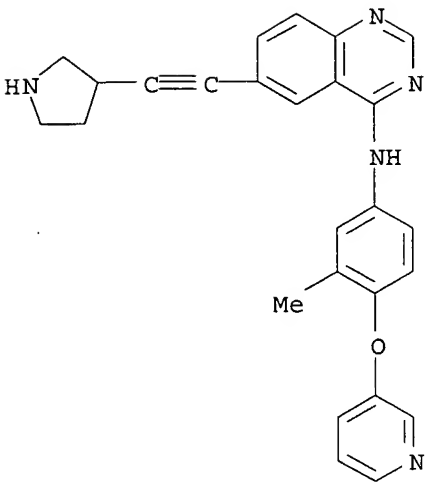
I

AB This invention relates to a method of treatment of cancer with a combination of an erbB2 ligand with formula I (where m = 0, 1, 2, 3; p = 0,1,2,3,4; R1 = H, C1-6 alkyl; R2 = H,C1-6 alkyl; R3 = 4 to 10 membered heterocyclic groups; R4 = alknyl, etc.; R5 = halo, OH, etc.; R11 = halo, cyano, etc.) and an antibody, in mammals. More particularly, this invention relates to a method of treating cancer by administering an erbB2 ligand in combination with an erbB antibody. This invention also relates to a kit useful in the treatment of abnormal cell growth in mammals, especially humans.

IT **383433-01-0P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(selective erbb2 inhibitor/anti-erbb antibody combinations in treatment of cancer)

RN 383433-01-0 CAPLUS

CN 4-Quinazolinamine, N-[3-methyl-4-(3-pyridinyloxy)phenyl]-6-(3-pyrrolidinylethynyl)- (9CI) (CA INDEX NAME)



L75 ANSWER 4 OF 14 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2005316548 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15833897
TITLE: Dopamine agonist-induced yawning in rats: a dopamine D3 receptor-mediated behavior.
AUTHOR: Collins Gregory T; Witkin Jeffrey M; Newman Amy H; Svensson Kjell A; Grundt Peter; Cao Jianjing; Woods James H
CORPORATE SOURCE: Department of Pharmacology, 1301 MSRB III, University of Michigan Medical School, Ann Arbor, MI 48109-0632, USA.
CONTRACT NUMBER: DA 00254 (NIDA)
DA 09161 (NIDA)
SOURCE: Journal of pharmacology and experimental therapeutics, (2005 Jul) 314 (1) 310-9. Electronic Publication: 2005-04-15.
Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article;. (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200508
ENTRY DATE: Entered STN: 20050621
Last Updated on STN: 20050827
Entered Medline: 20050826

AB A specific role for the dopamine D3 receptor in behavior has yet to be elucidated. We now report that dopamine D2/D3 agonists elicit dose-dependent yawning behavior in rats, resulting in an inverted U-shaped dose-response curve. A series of experiments was directed toward the hypothesis that the induction of yawning is a D3 receptor-mediated effect, whereas the inhibition of the yawning observed at higher doses is due to competing D2 receptor activity. We compared several dopaminergic agonists with a range of in vitro D3 selectivity, including PD-128,907 [(S)-(+)-(4aR, 10bR)-3,4,4a,10b-tetrahydro-4-propyl-2H,5H-[1]benzopyrano-[4,3-b]-1,4-oxazin-9-ol HCl], PD-128,908 [(R)-(-)-(4aS,10bS)-3,4,4a,10b-tetrahydro-4-propyl-2H,5H-[1]benzopyrano-[4,3-b]-1,4-oxazin-9-ol HCl], quinelorane [(5aR-trans)-5,5a,6,7,8, 9,9a,10-octahydro-6-propylpyrido[2,3-g]**quinazolin**-2-**amine** dihydrochloride], pramipexole (N'-propyl-4,5,6,7-tetrahydrobenzothiazole-2,6-diamine), 7-OH-DPAT [(+/-)-7-hydroxy-2-dipropylaminotetralin HBr], quinpirole [trans-(-)-(4aR)-4,4a,5,6,7,8, 8a,9-octahydro-5-propyl-1H-pyrazolo[3,4-

g]quinoline HCl], bromocriptine [(+)-2-bromo-12'-hydroxy-2'-(1-methylethyl)-5'-(2-methylpropyl) ergotaman-3',6'-18-trione methanesulfonate], and apomorphine [(R)-(-)-5,6,6a,7-tetrahydro-6-**methyl**-4H-dibenzo-[de,g]quinoline-10,11-diol HCl] with respect to their ability to induce yawning in rats. A series of D2/D3 antagonists differing in selectivity for D3 over D2 receptors were evaluated for their ability to alter the effects of the dopamine agonists. The antagonists L-741,626 (3-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]**methyl**-1H-indole), haloperidol (4-[4-(4-chlorophenyl)-4-hydroxy-1-piperidinyl]-1-(4-fluorophenyl)-1-butanone HCl), nafadotride (N-[(1-butyl-2-**pyrrolidinyl**)**methyl**]-4-cyano-1-**methoxy**-2-naphtha-lenecarboxamide), U99194 (2,3-dihydro-5,6-dimethoxy-N,N-dipropyl-1H-inden-2-**amine** maleate), SB-277011A (trans-N-[4-[2-(6-cyano-1,2,3,4-tetrahydroisoquinolin-2-yl)ethyl]cyclohexyl]-4-quinolinecarboxamide), and PG01037 (N-{4-[4-(2,3-dichlorophenyl)-piperazin-1-yl]-trans-but-2-enyl}-4-**pyridine**-2-yl-benzamide HCl) were used to determine effects on dose-response curves for D2/D3 agonist-induced yawning. In addition, the potential contribution of cholinergic and/or serotonergic mechanisms to the yawning response was investigated using a series of pharmacological tools including scopolamine [(a,S)-a-(hydroxymethyl)benzeneacetic acid (1a,2b,4b,5a,7b)-9-**methyl**-3-oxa-9-azatricyclo[3.3.1.02,4]-non7-yl ester hydrobromide], mianserin (1,2,3,4,10,14b-hexahydro-2-methyldibenzo[c,f]pyrazino[1,2-a]azepine HCl), and the D3-preferring antagonists nafadotride, U99194, SB-277011A, and PG01037 to differentially modulate yawning induced by PD-128,907, physostigmine [(3aS)-cis-1,2,3,3a,8,8a-hexahydro-1,3a,8-trimethylpyrrolo[2,3-b]indol-5-ol methylcarbamate hemisulfate], and N-[3-(trifluoromethyl)phenyl]piperazine HCl. The results of these experiments provide convergent evidence that dopamine D2/D3 agonist-induced yawning is a D3 agonist-mediated behavior, with subsequent inhibition of yawning being driven by competing D2 agonist activity. Thus, dopamine agonist-induced yawning may represent an in vivo method for selectively identifying D3 and D2 receptor-mediated activities.

L75 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:780693 CAPLUS
DOCUMENT NUMBER: 141:296042
TITLE: Preparation of quinazolines non-receptor tyrosine kinase inhibitors as antitumor agents
INVENTOR(S): Barlaam, Bernard
PATENT ASSIGNEE(S): AstraZeneca AB, Swed.; AstraZeneca UK Limited
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004081000	A1	20040923	WO 2004-GB942	20040305

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,

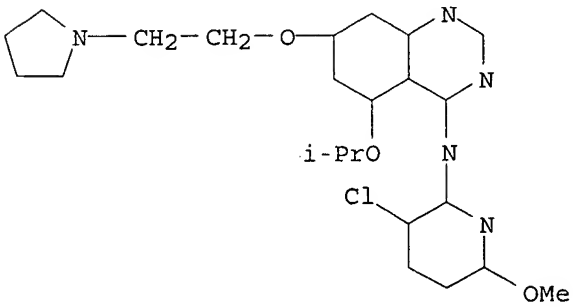
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: EP 2003-290581 A 20030310
OTHER SOURCE(S): MARPAT 141:296042
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title quinazolines I [wherein Z = O, S, SO, SO2, NR2, CR2R3; R2, R3 = independently H, alkyl; m = 1-3; R1 = independently halo, CF3, CN, NC, NO2, OH, SH, NH2, CHO, CO2H, carbamoyl, sulfamoyl, alk(en/yn)yl, etc.; Ra = H, halo; Rb, Rc = independently H, halo, alkyl, alkoxy; Rd = alkoxy; or their pharmaceutically acceptable salts thereof] were prepared as non-receptor tyrosine kinase inhibitors. For example, 4-chloro-7-(2-chloroethoxy)-6-methoxyquinazoline (preparation given) was coupled with 2-amino-3-chloro-6-methoxypyridine using sodium hexamethyldisilazane in DMF to give II. Selected I inhibited the phosphorylation of a tyrosine containing polypeptide substrate by human recombinant c-Src kinase (IC50 in the range of 0.001-0.5 μM), suppressed the proliferation of mouse 3T3 fibroblast cells stably-transfected with an activating mutant of human c-Src (IC50 in the range of 0.1-5 μM), and inhibited the migration of the human tumor cell line A549 (IC50 in the range of 0.1-5 M). In addition, no physiol. unacceptable toxicity was observed at the ED for compds. tested in an in vivo A549 xenograft growth assay using athymic nude mice. Thus, I and pharmaceutical compns. containing them are useful as anti-invasive agents in the containment and/or treatment of solid tumor disease.

IT **763123-88-2P**, 4-[(3-Chloro-6-methoxypyridin-2-yl)amino]-5-isopropoxy-7-[2-(pyrrolidin-1-yl)ethoxy]quinazoline **763123-93-9P**, 4-[(3-Chloro-6-methoxypyridin-2-yl)amino]-5-isopropoxy-7-[3-(pyrrolidin-1-yl)propoxy]quinazoline
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antitumor agent; preparation of quinazolines c-Src kinase inhibitors as antitumor agents)

RN 763123-88-2 CAPLUS
CN 4-Quinazolinamine, N-(3-chloro-6-methoxy-2-pyridinyl)-5-(1-methylethoxy)-7-[2-(1-pyrrolidinyl)ethoxy]- (9CI) (CA INDEX NAME)

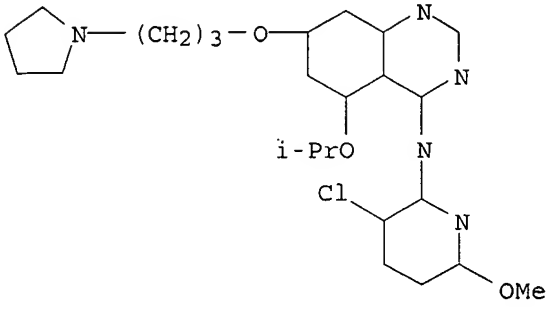


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 763123-93-9 CAPLUS
CN 4-Quinazolinamine, N-(3-chloro-6-methoxy-2-pyridinyl)-5-(1-methylethoxy)-7-

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

[3-(1-pyrrolidinyl)propoxy]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

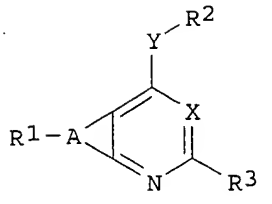
L75 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:633933 CAPLUS
DOCUMENT NUMBER: 141:174181
TITLE: Preparation of quinolines, quinazolines and thienopyrimidines as ALK-5 receptor ligands for the treatment of kidney fibrosis
INVENTOR(S): Dodic, Nerina; Gellibert, Francoise Jeanne; Hunter, Robert Neil, III
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004065392	A1	20040805	WO 2004-EP650	20040126
WO 2004065392	C1	20041007		

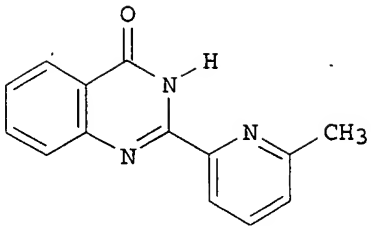
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

PRIORITY APPLN. INFO.:	GB 2003-1719	A	20030124
	GB 2003-8706	A	20030415
	GB 2003-15519	A	20030702

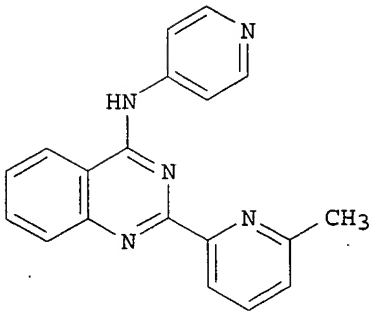
OTHER SOURCE(S): MARPAT 141:174181
GI



I



II



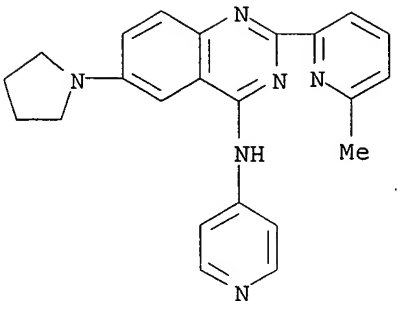
III

AB Condensed pyridines and pyrimidines (quinolines, quinazolines and thienopyrimidines) of formula I [X is N or CH; Y is -NR- or -NHCH2-; R is alkyl; A is a fused 5-7 membered carbocyclic or N/O/S-heterocyclic ring with one or more R1 groups; R1 is H, halo, NO2, alkyl, OR, CONR4R5, O(CH2)nNR4R5, (CH2)nNR4R5, or NR4R5; R2 is certain N-containing heterocyclic rings; R3 is pyridin-2-yl, C1-6alkyl-pyridin-2-yl, -pyrrol-2-yl or -thiazol-2-yl; R4 is H or alkyl; R5 is alkyl; NR4R5 can be 3-7 membered (un)saturated N/O/S-heterocycle] and their pharmaceutically acceptable salts, solvates or derivs. were synthesized. Thus, 2-aminobenzamide was coupled with 6-methyl-2-pyridinecarboxylic acid in the presence of EDCI/HOBT followed by cyclocondensation mediated by NaOH to give quinazolinone II. Chlorination of II with POCl3 and subsequent substitution of the resulting chloride with 4-aminopyridine afforded quinazoline III. These compds. are inhibitors of the transforming growth factor TGF-β, especially of activin-like kinase ALK-5 receptor, and are used in the treatment and prevention of various disease states mediated by ALK-5 kinase mechanisms such as kidney fibrosis. All the final products showed ALK5 receptor modulator activity with IC50 of 1-200 nM (16 nM for III) and TGF-β cellular activity with IC50 of 0.001-10 μM (82 nM for III). The role of ALK5 inhibitors for the treatment of photoaging was also demonstrated exptl.

IT **733806-97-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of quinolines, quinazolines and thienopyrimidines as ALK-5 receptor ligands for the treatment of, e.g., kidney fibrosis)

RN 733806-97-8 CAPLUS

CN 4-Quinazolinamine, 2-(6-methyl-2-pyridinyl)-N-4-pyridinyl-6-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:546501 CAPLUS
DOCUMENT NUMBER: 141:106486
TITLE: Preparation of 4-(pyridin-4-ylamino)quinazolines as antitumor agents
INVENTOR(S): Barlaam, Bernard
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004056812	A1	20040708	WO 2003-GB5534	20031218
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2002-293220 A 20021223
OTHER SOURCE(S): MARPAT 141:106486
GI

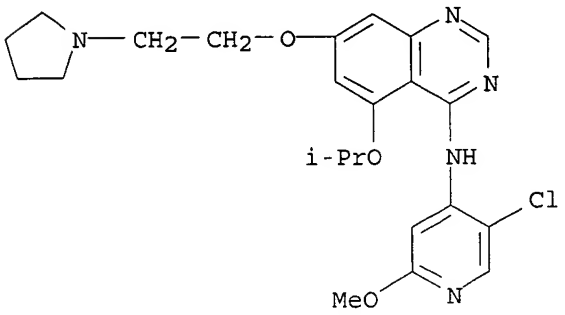
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Quinazolines I [Z = O, S, SO, SO2, (un)substituted NH2, CH2; m =1, 2 3; R1 = halogen, CF3, CN, NO2, (un)substituted OH, SH, NH2, CHO, CO2H, CONH2, alkyl, alkenyl, alkynyl, SO2NH2; R2 = H, halogen; R3, R5 = H, halogen, alkyl, alkoxy; R4 = alkoxy] were prepared for use as an anti-invasive agent in the containment and/or treatment of solid tumor disease (no data). Thus, 5-chloro-2-methoxypyridine was converted to its N-oxide, nitrated to 5-chloro-2-methoxy-4-nitropyridine and reduced to the amine which was

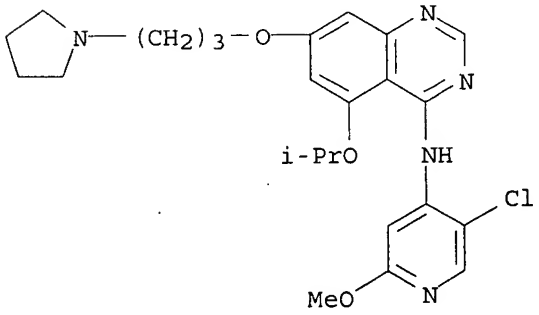
treated with the 4-chloroquinazoline fragment to give the quinazoline II. The chloroquinazoline fragment was prepared by treating 5,7-difluoro-3,4-dihydroquinazolin-4-one with 4-tetrahydropyranol followed by 1-(2-hydroxyethyl)piperazine and acetylation.

IT **719305-08-5P 719305-13-2P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-(pyridin-4-ylamino)quinazolines as antitumor agents)

RN 719305-08-5 CAPLUS
CN 4-Quinazolinamine, N-(5-chloro-2-methoxy-4-pyridinyl)-5-(1-methylethoxy)-7-[2-(1-pyrrolidinyl)ethoxy]- (9CI) (CA INDEX NAME)



RN 719305-13-2 CAPLUS
CN 4-Quinazolinamine, N-(5-chloro-2-methoxy-4-pyridinyl)-5-(1-methylethoxy)-7-[3-(1-pyrrolidinyl)propoxy]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:546495 CAPLUS
DOCUMENT NUMBER: 141:106483
TITLE: Preparation of quinazoline derivatives as antitumor agents
INVENTOR(S): Barlaam, Bernard
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004056801	A1	20040708	WO 2003-GB5540	20031218

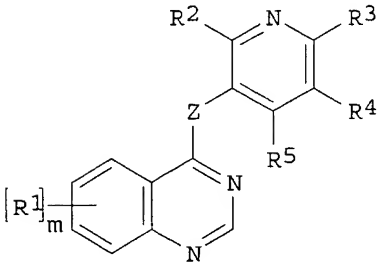
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2002-293221 A 20021223

OTHER SOURCE(S): MARPAT 141:106483

GI



I

AB The title compds. I [Z = O, S, SO, SO2, NR2, CR2R3 (wherein R2, R3 = H, alkyl); m = 1-3; R1 = halo, alkyl, alkoxy, etc.; R2 = H, halo; R3 = H, halo, alkyl, alkoxy; R4 = alkoxy; R5 = H, halo, alkyl, alkoxy; or pharmaceutically-acceptable salts thereof], useful as an anti-invasive agent in the containment and/or treatment of solid tumor disease, were prepared E.g., a multi-step synthesis of 7-(2-chloroethoxy)-4-(2-chloro-5-methoxypyridin-3-ylamino)-6-methoxyquinazoline, was given. The exemplified compds. I were evaluated in four biol. tests. For example, they showed IC50 of 0.001-0.5 μM in in vitro assay for inhibiting phosphorylation of a tyrosine containing polypeptide substrate by the enzyme c-Src kinase. The pharmaceutical composition comprising the compound I is claimed.

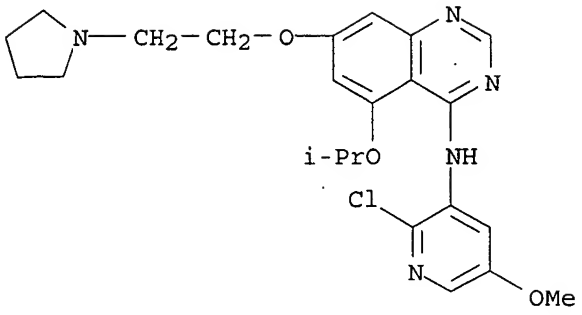
IT **720666-36-4P 720666-41-1P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

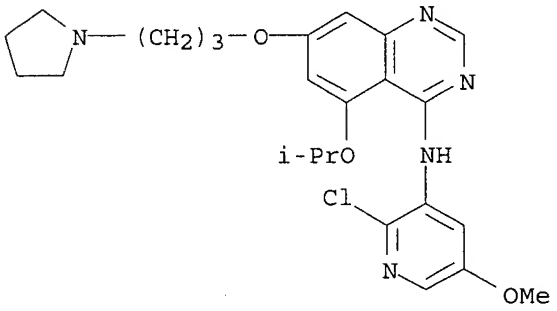
(preparation of quinazoline derivs. as antitumor agents)

RN 720666-36-4 CAPLUS

CN 4-Quinazolinamine, N-(2-chloro-5-methoxy-3-pyridinyl)-5-(1-methylethoxy)-7-[2-(1-pyrrolidinyl)ethoxy]- (9CI) (CA INDEX NAME)



RN 720666-41-1 CAPLUS
CN 4-Quinazolinamine, N-(2-chloro-5-methoxy-3-pyridinyl)-5-(1-methylethoxy)-7-[3-(1-pyrrolidinyl)propoxy]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:534191 CAPLUS
DOCUMENT NUMBER: 141:89100
TITLE: Preparation of (quinazolin-4-yl)amines as capsaicin receptor modulators
INVENTOR(S): Bakthavatchalam, Rajagopal; Blum, Charles A.; Brielmann, Harry; Caldwell, Timothy M.; De Lombaert, Stephane; Hodgetts, Kevin J.; Zheng, Xiaozhang
PATENT ASSIGNEE(S): Neurogen Corporation, USA
SOURCE: PCT Int. Appl., 226 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004055003	A1	20040701	WO 2003-US39606	20031212

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

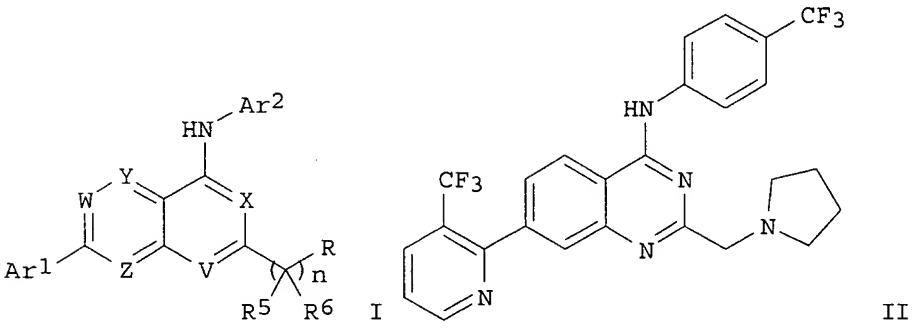
CA 2509233	AA	20040701	CA 2003-2509233	20031212
US 2004156869	A1	20040812	US 2003-735607	20031212
EP 1569925	A1	20050907	EP 2003-813410	20031212

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.: US 2002-433139P P 20021213
WO 2003-US39606 W 20031212

OTHER SOURCE(S): MARPAT 141:89100

GI



I II

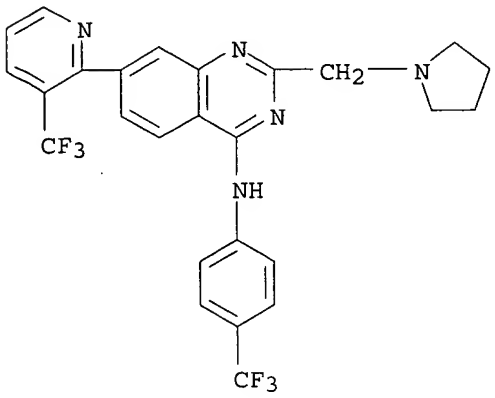
AB Title compds. I [wherein V, W, X, Y, and Z = independently N, CR1, with the proviso that at least one of V and X = N; R = OR7, NR3R4; R1 = independently H, halo, OH, CN, NH2, (halo)alkyl, (halo)alkoxy, alkoxycarbonyl, (di)alkylamino; R3 and R4 = independently H, (un)substituted (aryl)alkyl, alkenyl, alkynyl, alkanoyl, etc.; or R3 or R4 taken together with R5 or R6 forms an (un)substituted heterocycle; or NR3R4 = heterocyclyl; R5 and R6 = independently H, (un)substituted alkyl; or CR5R6 = CO; R7 = H, (aryl)alkyl, alkenyl, alkynyl, alkanoyl, etc.; or R7 taken together with R5 or R6 forms an (un)substituted heterocycle; n = 1-3; Ar1 and Ar2 = independently (un)substituted aryl, heterocyclyl; and pharmaceutically acceptable forms thereof] were prepared as modulators of capsaicin receptors, especially the vanilloid receptor 1 (VR1). For example, a solution of [2-(chloromethyl)-7-(3-trifluoromethylpyridin-2-yl)quinazolin-4-yl](4-trifluoromethylphenyl)amine•HCl and pyrrolidine was heated to 100° for 1 h to give II. In competition binding assays, invention compds. exhibited Ki ≤ 1 μM for VR1 expressed in human embryonic kidney (HEK293) cells. Thus, I and their pharmaceutical compns. are useful for treating disorders associated with pathol. receptor activation, such as pain, in humans, domesticated companion animals, and livestock animals (no data).

IT **573680-38-3P 573681-61-5P 573683-59-7P 573685-18-4P 573686-42-7P 573688-13-8P 573688-67-2P 573688-69-4P**

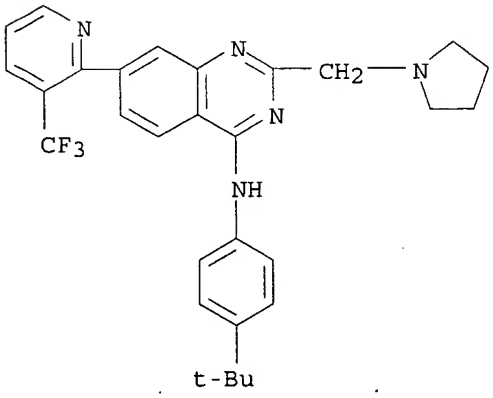
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(VR1 inhibitor; preparation of (quinazolin-4-yl)amines as VR1 inhibitors for treatment of pain and other VR1-mediated conditions)

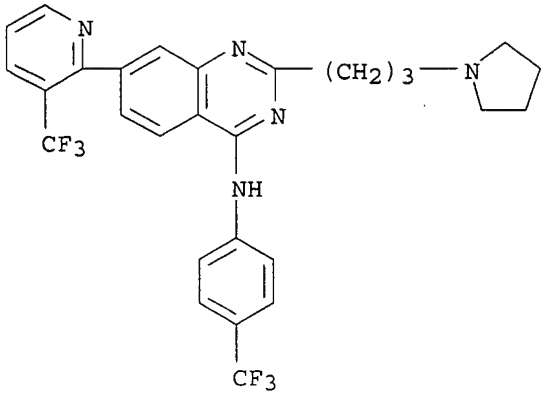
RN 573680-38-3 CAPLUS
CN 4-Quinazolinamine, 2-(1-pyrrolidinylmethyl)-N-[4-(trifluoromethyl)phenyl]-7-[3-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



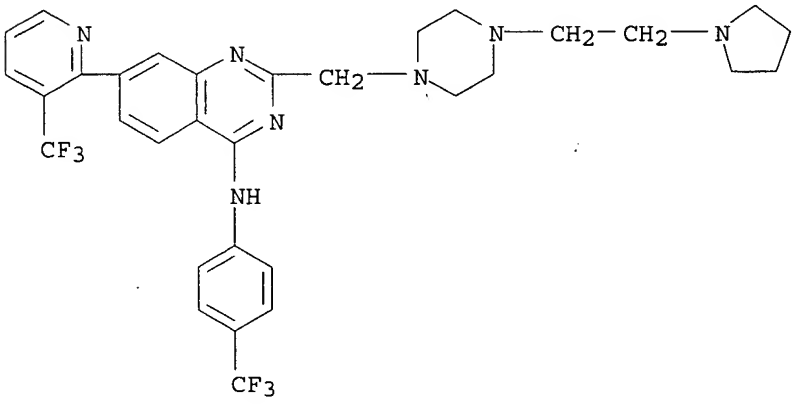
RN 573681-61-5 CAPLUS
CN 4-Quinazolinamine, N-[4-(1,1-dimethylethyl)phenyl]-2-(1-pyrrolidinylmethyl)-7-[3-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



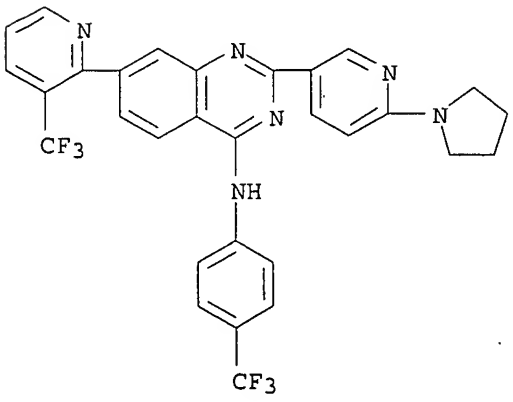
RN 573683-59-7 CAPLUS
CN 4-Quinazolinamine, 2-[3-(1-pyrrolidinyl)propyl]-N-[4-(trifluoromethyl)phenyl]-7-[3-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



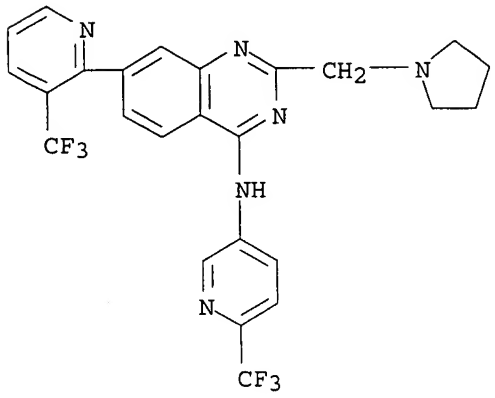
RN 573685-18-4 CAPLUS
CN 4-Quinazolinamine, 2-[[4-[2-(1-pyrrolidinyl)ethyl]-1-piperazinyl]methyl]-N-[4-(trifluoromethyl)phenyl]-7-[3-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



RN 573686-42-7 CAPLUS
CN 4-Quinazolinamine, 2-[6-(1-pyrrolidinyl)-3-pyridinyl]-N-[4-(trifluoromethyl)phenyl]-7-[3-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)

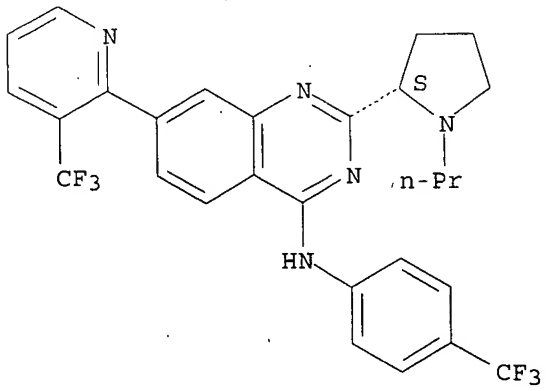


RN 573688-13-8 CAPLUS
CN 4-Quinazolinamine, 2-(1-pyrrolidinylmethyl)-7-[3-(trifluoromethyl)-2-pyridinyl]-N-[6-(trifluoromethyl)-3-pyridinyl]- (9CI) (CA INDEX NAME)



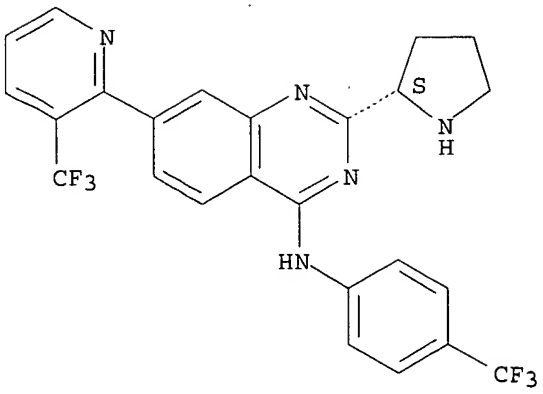
RN 573688-67-2 CAPLUS
CN 4-Quinazolinamine, 2-[(2S)-1-propyl-2-pyrrolidinyl]-N-[4-(trifluoromethyl)phenyl]-7-[3-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 573688-69-4 CAPLUS
CN 4-Quinazolinamine, 2-(2S)-2-pyrrolidinyl-N-[4-(trifluoromethyl)phenyl]-7-[3-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



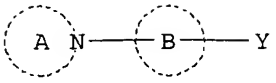
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:515487 CAPLUS
DOCUMENT NUMBER: 141:71555
TITLE: Preparation of nitrogen-containing heterocyclic compounds as CXCR4 regulators
INVENTOR(S): Habashita, Hiromu; Kokubo, Masaya; Shibayama, Shiro; Tada, Hideaki; Tanihiro, Tatsuya
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 641 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

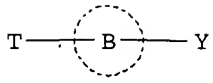
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004052862	A1	20040624	WO 2003-JP15718	20031209
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1571146	A1	20050907	EP 2003-778753	20031209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.:
JP 2002-357446 A 20021210
JP 2003-162706 A 20030606
WO 2003-JP15718 W 20031209

OTHER SOURCE(S): MARPAT 141:71555
GI



I



II

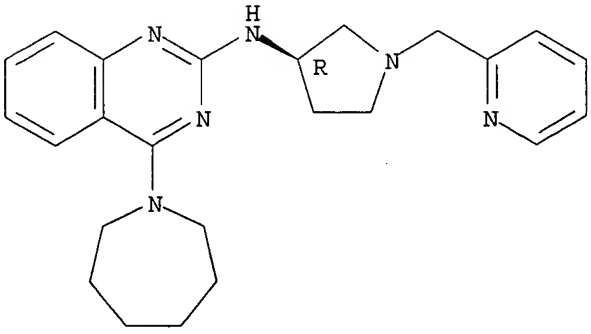
AB Compds. such as pyrimidine and quinazoline derivs. represented by the following general formulas (I) and (II), salts thereof, N-oxides thereof, solvates thereof or prodrugs of the same (wherein the ring A represents an optionally substituted nitrogen-containing heterocycle; the ring B represents an optionally substituted homocycle or an optionally substituted heterocycle; Y represents an optionally substituted hydrocarbyl group, an optionally substituted heterocyclic group, an optionally protected amino group, an optionally protected hydroxyl group or an optionally protected mercapto group; and T represents the ring A or an optionally substituted amino group) are prepared These compds. are CXCR4 regulators, in particular CXCR4 antagonists, and useful as preventives and/or remedies for various inflammatory diseases, immune diseases, various allergic diseases, infectious diseases, acquired immunodeficiency syndrome, infection with human immunodeficiency virus, psychiatric disorder, neurol. disease, cerebral diseases, cardiovascular diseases, metabolic diseases, or cancer, and agents for regeneration therapy, in particular transplant therapy. An assay system using SDF-1 which is an endogenous ligand of CXCR4 receptor, instead of HIV, was used in an assay for screening compds. which inhibit the binding of HIV to CXCR4 or CCR4 receptors on CD4-pos. cells. All the compds. prepared showed IC50 of 10 μM for inhibiting the binding of [125I]human SDF-1 to CEM cells, more specifically 0.1 μM for 2-(1-benzylpyrrolidin-3-ylamino)-4-(perhydroazepin-1-yl)pyrimidine. An ampule and tablet formulation containing 2-[[2-(dimethylamino)ethyl]amino]-4-(perhydroazepin-1-yl)pyrimidine were described.

IT **710998-73-5P 710998-77-9P 710999-09-0P**
711000-03-2P 711000-04-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitrogen-containing heterocyclic compds. as CXCR4 antagonists
for preparation and/treatment of diseases)

RN 710998-73-5 CAPLUS

CN 2-Quinazolinamine, 4-(hexahydro-1H-azepin-1-yl)-N-[(3R)-1-(2-pyridinylmethyl)-3-pyrrolidinyl]- (9CI) (CA INDEX NAME)

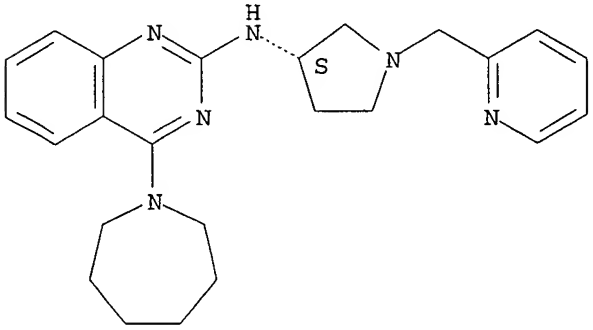
Absolute stereochemistry.



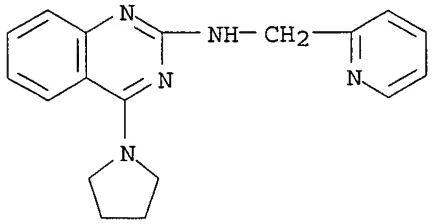
RN 710998-77-9 CAPLUS

CN 2-Quinazolinamine, 4-(hexahydro-1H-azepin-1-yl)-N-[(3S)-1-(2-pyridinylmethyl)-3-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

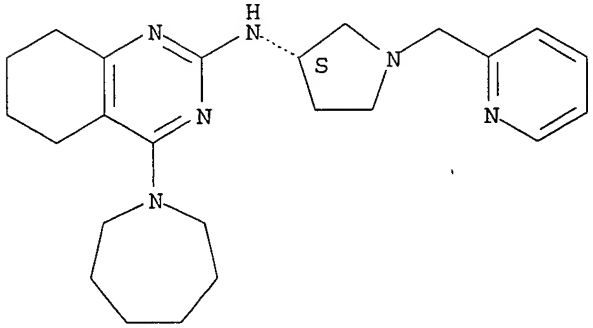


RN 710999-09-0 CAPLUS
CN 2-Quinazolinamine, N-(2-pyridinylmethyl)-4-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



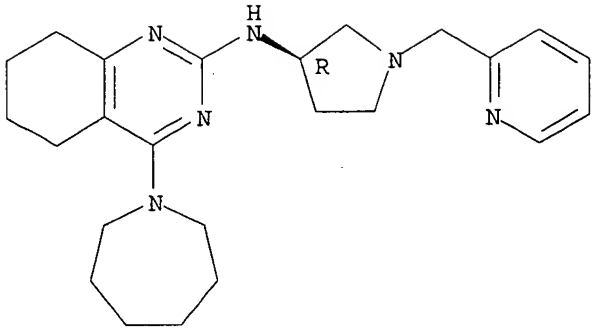
RN 711000-03-2 CAPLUS
CN 2-Quinazolinamine, 4-(hexahydro-1H-azepin-1-yl)-5,6,7,8-tetrahydro-N-[(3S)-1-(2-pyridinylmethyl)-3-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 711000-04-3 CAPLUS
CN 2-Quinazolinamine, 4-(hexahydro-1H-azepin-1-yl)-5,6,7,8-tetrahydro-N-[(3R)-1-(2-pyridinylmethyl)-3-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L75 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:430753 CAPLUS
DOCUMENT NUMBER: 141:1220
TITLE: Preparation of quinazolines as Src family non-receptor tyrosine kinase inhibitors for use in combination therapy with gemcitabine for treatment and prophylaxis of pancreatic cancer
INVENTOR(S): Barge, Alan
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004043472	A1	20040527	WO 2003-GB4787	20031107
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2504666	AA	20040527	CA 2003-2504666	20031107
EP 1562612	A1	20050817	EP 2003-772404	20031107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003016170	A	20050927	BR 2003-16170	20031107

PRIORITY APPLN. INFO.:
GB 2002-26434 A 20021113
WO 2003-GB4787 W 20031107

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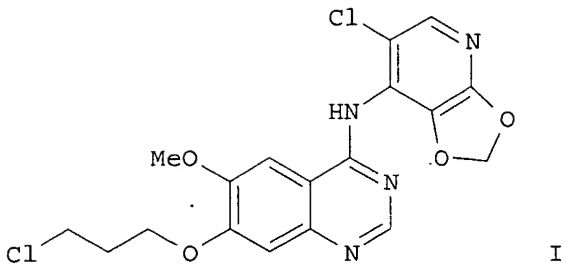


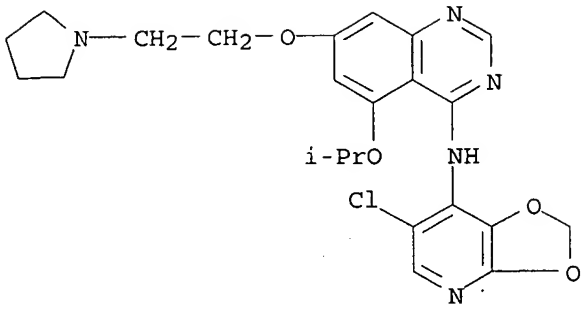
I

AB The invention concerns a combination comprising an inhibitor of Src kinase and the cytotoxic agent, gemcitabine, a pharmaceutical composition comprising such a combination, and its use in the treatment or prophylaxis of cancer, particularly of pancreatic cancer. Examples include prepns. for anilino- and (pyridylamino)quinazoline Src inhibitors (no Markush structure given) and bioassays demonstrating the synergistic effect of treating pancreatic cancer with a quinazoline Src inhibitor in combination with gemcitabine. For instance, 4-amino-5-chloro-2,3-methylenedioxypyridine was coupled with 4-chloro-7-(3-chloropropoxy)-6-methoxyquinazoline (preparation of reactants given) in the presence of sodium hexamethyldisilazane in THF to afford the (pyridylamino)quinazoline I. Nude mice were injected with pancreatic tumor cells derived from the COLO 357 human pancreatic cancer cell line and treated with gemcitabine, the Src inhibitor, 4-(2-chloro-5-methoxyanilino)-6-methoxy-7-(N-methylpiperidin-4-ylmethoxy)quinazoline, or a combination of the two. Evaluation for tumor growth and incidence of liver metastases showed that, compared with the weight of control tumors, tumor growth in animals treated with the combination was much reduced (1359 mg and 124 mg, resp.) to a level well below that achievable on the dosing of either gemcitabine or the Src inhibitor alone. In addition, there was no liver metastasis in the animals treated with the combination, whereas liver metastasis was present in 1/5 of the animals treated with gemcitabine alone.

IT **692055-41-7P**, 5-Isopropoxy-7-[2-(pyrrolidin-1-yl)ethoxy]-4-[(5-chloro-2,3-methylenedioxypyridin-4-yl)amino]quinazoline
692055-66-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antitumor agent; preparation of quinazoline-containing Src inhibitors for use
in synergistic combination with gemcitabine for treatment and prophylaxis of pancreatic cancer)

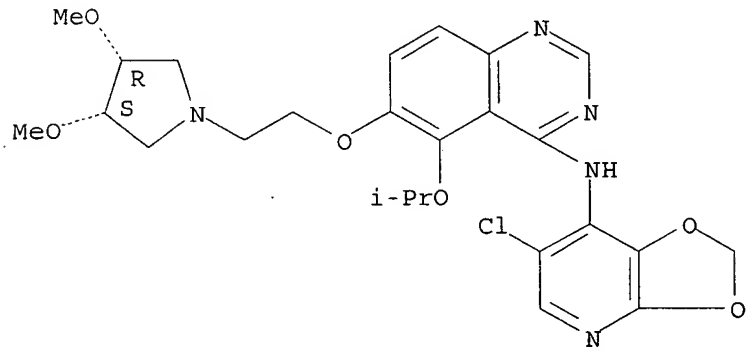
RN 692055-41-7 CAPLUS

CN 4-Quinazolinamine, N-(6-chloro-1,3-dioxolo[4,5-b]pyridin-7-yl)-5-(1-methylethoxy)-7-[2-(1-pyrrolidinyl)ethoxy]- (9CI) (CA INDEX NAME)



RN 692055-66-6 CAPLUS
CN 4-Quinazolinamine, N-(6-chloro-1,3-dioxolo[4,5-b]pyridin-7-yl)-6-[2-[(3R,4S)-3,4-dimethoxy-1-pyrrolidinyl]ethoxy]-5-(1-methylethoxy)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:414727 CAPLUS
DOCUMENT NUMBER: 140:423698
TITLE: Preparation of quinazoline derivatives as c-Src tyrosine kinase inhibitors
INVENTOR(S): Ple, Patrick
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.; Astrazeneca Uk Limited
SOURCE: PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004041829	A1	20040521	WO 2003-GB4703	20031029

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,

		OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	TJ,	TM,
		TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW		
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,
		KG,	KZ,	MD,	RU,	TJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
		FI,	FR,	GB,	GR,	HU,	IE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	TR,
		BF,	BJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG
CA 2503371					AA		20040521		CA 2003-2503371						20031029		
EP 1562955					A1		20050817		EP 2003-769689						20031029		
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
		IE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR,	BG,	CZ,	EE,	HU,	SK	
BR 2003015756					A		20050906		BR 2003-15756						20031029		
PRIORITY APPLN. INFO.:									EP 2002-292736					A	20021104		
									EP 2003-290900					A	20030410		
									WO 2003-GB4703					W	20031029		

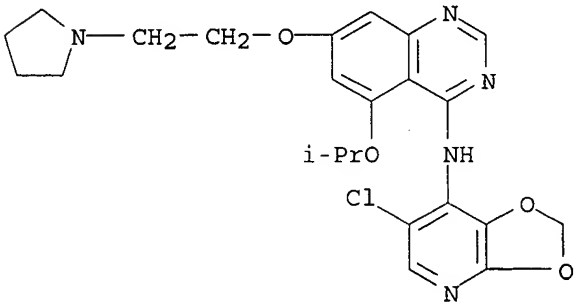
OTHER SOURCE(S): MARPAT 140:423698
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. I [R1 = halo, CF3, cyano, isocyano, NO3, OH, SH, amino, formyl, carboxy, carbamoyl, alkyl, alkenyl, alkynyl, alkoxy, etc.; Z = O, SO, SO2, N(R2)2, or C(R2)2; R2 = H or alkyl; m = 0-3; R3 = halo, CF3, CN, NO2, OH, amino, carboxy, carbamoyl, alkyl, alkenyl, alkynyl, alkoxy, etc.; n =0-3] were prepared as c-Src tyrosine kinase inhibitors in the containment and/or treatment of solid tumor disease. For example, reaction of 4-amino-5-chloro-2,3-methylenedioxypyridine(preparation given) and 4-chloro-7-(3-chloropropoxy)-6-methoxyquinazoline (preparation given) yielded compound II.

IT **692055-41-7P 692055-66-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinazoline derivs. as c-Src tyrosine kinase inhibitors)

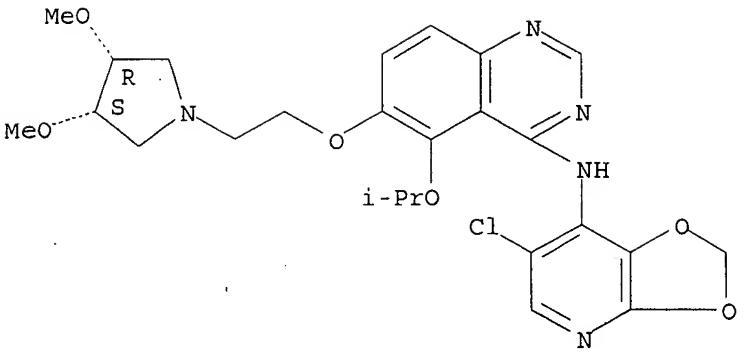
RN 692055-41-7 CAPLUS
CN 4-Quinazolinamine, N-(6-chloro-1,3-dioxolo[4,5-b]pyridin-7-yl)-5-(1-methylethoxy)-7-[2-(1-pyrrolidinyl)ethoxy]- (9CI) (CA INDEX NAME)



RN 692055-66-6 CAPLUS
CN 4-Quinazolinamine, N-(6-chloro-1,3-dioxolo[4,5-b]pyridin-7-yl)-6-[2-[(3R,4S)-3,4-dimethoxy-1-pyrrolidinyl]ethoxy]-5-(1-methylethoxy)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86



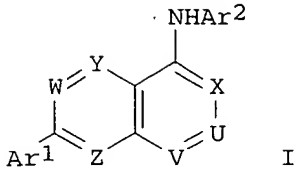
L75 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:591156 CAPLUS
DOCUMENT NUMBER: 139:149640
TITLE: Preparation of substituted quinazolin-4-ylamine analogs as VR1 capsaicin receptor antagonists for relieving pain
INVENTOR(S): Bakthavatchatam, Rajagopal; Blum, Charles A.; Brielmann, Harry L.; Caldwell, Timothy M.; De Lombaert, Stephane
PATENT ASSIGNEE(S): Neurogen Corporation, USA
SOURCE: PCT Int. Appl., 294 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003062209	A2	20030731	WO 2003-US1563		20030117
WO 2003062209	A3	20030904			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2473796	AA	20030731	CA 2003-2473796		20030117
BR 2003006982	A	20041026	BR 2003-6982		20030117
EP 1471910	A2	20041103	EP 2003-703887		20030117
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2005526714	T2	20050908	JP 2003-562090		20030117
US 2004106616	A1	20040603	US 2003-347210		20030121
NO 2004003411	A	20040924	NO 2004-3411		20040816
PRIORITY APPLN. INFO.:			US 2002-349920P	P	20020117
			US 2002-350527P	P	20020122
			WO 2003-US1563	W	20030117

OTHER SOURCE(S): MARPAT 139:149640

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

GI



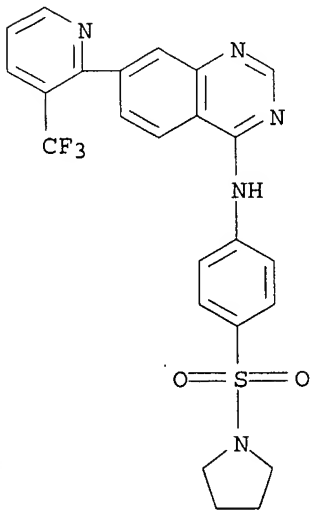
I

AB Substituted quinazolin-4-ylamine analogs (shown as I; variables defined below; e.g. (4-trifluoromethylphenyl)[7-(2-trifluoromethylphenyl)quinazolin-4-yl]amine) are provided. Such compds. are ligands that may be used to modulate VR1 capsaicin receptor activity in vivo or in vitro (no data), and are particularly useful in the treatment of conditions associated with pathol. receptor activation in humans, domesticated companion animals and livestock animals. Pharmaceutical compns. and methods for using them to treat such disorders are provided, as are methods for using such ligands for receptor localization studies. For I; V, X, W, Y and Z are each independently N or CR1, with the proviso that at least one of V and X is N; U is N or CR2, with the proviso that if V and X are N, then U is CR2; R1 = H, halogen, hydroxy, amino, C1-C8 alkyl, haloC1-C8alkyl, C1-C8alkoxy, haloC1-C8alkoxy and mono- and di(C1-C8alkyl)amino. R2 = (i) H, halogen, cyano, or -COOH; (ii) C1-C8alkanoyl, C2-C8alkanone, or C1-C8carbamate, each of which is (un)substituted with 1-9 substituents = Rb, or (iii) -Rc-M-A-Ry, wherein: Rc is C0-C3alkyl; M is a bond, N(Rz), O, S, SO2, (C:O)pN(Rz), N(Rz)(C:O)p, SO2N(Rz), or N(Rz)SO2, wherein p is 0 or 1; A is a bond or C1-C8alkyl, (un)substituted with 1-3 Rb. Ry and Rz, if present, are: (a) independently H, C1-C8alkyl, C2-C8alkenyl, C2-C8alkynyl, C6-C10arylC1-C8alkyl, C2-C8alkyl ether, C1-C8alkoxy, a 4- to 10-membered carbocycle or heterocycle, or joined to R1 to form a 4- to 10-membered carbocycle or heterocycle, wherein each Ry and Rz = (un)substituted with 1-9 Rb; or (b) joined to form a 4- to 10-membered carbocycle or heterocycle that is (un)substituted with 1-9 Rb; Ar2 is a 5- to 7-membered aromatic heterocycle, (un)substituted with 1-3 LRa. Ar1 is a 5- to 10-membered aromatic carbocycle or heterocycle, (un)substituted with 1-3 LRa; L = bond, -O-, -C(O)-, -OC(O)-, -C(O)O-, -O-C(O)O-, -S(O)m-, -NRx-, -C(O)NHRx-, -NHRxC(O)-, -NRxS(O)m-, -S(O)mNRx- and -N[S(O)mRx]S(O)m-; wherein m = 0, 1 and 2; and Rx = H and C1-C8alkyl; Ra = (i) H, halogen, cyano and nitro; and (ii) C1-C8alkyl, C2-C8alkenyl, C2-C8alkynyl, C2-C8alkyl ether, 3- to 10-membered heterocycles, mono- and di(C1-C8alkyl)amino and (3- to 10-membered heterocycle)C1-C6 alkyl, each of which is (un)substituted with 1-9 Rb. Rb = hydroxy, halogen, amino, aminocarbonyl, amido, cyano, nitro, C1-C8alkyl, C1-C8alkoxy, C1-C8alkylthio, C1-C8alkyl ether, hydroxyC1-C8alkyl, haloC1-C8alkyl, Ph, phenyl(C1-C8alkyl), mono and di(C1-C6 alkyl)amino, (SO2)C1-C8alkyl, 5- to 7-membered heterocycle and (5- to 7-membered heterocycle)(C1-C8alkyl). Although the methods of preparation are not claimed, many example prepns. and characterization data for >500 examples of I are included.

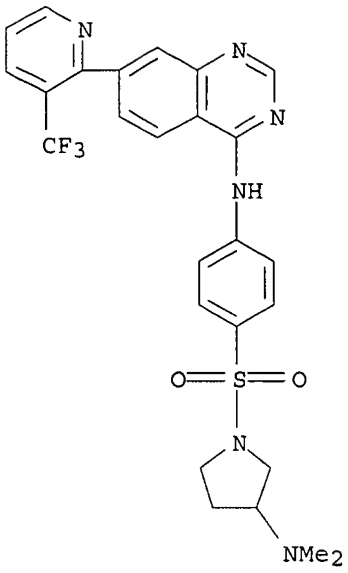
IT **573676-82-1P**, [4-[(Pyrrolidin-1-yl)sulfonyl]phenyl][7-(3-trifluoromethylpyridin-2-yl)quinazolin-4-yl]amine **573676-84-3P**, [4-[(3-Dimethylaminopyrrolidin-1-yl)sulfonyl]phenyl][7-(3-trifluoromethylpyridin-2-yl)quinazolin-4-yl]amine **573676-96-7P**, [4-[(2-Methylpyrrolidin-1-yl)sulfonyl]phenyl][7-(3-trifluoromethylpyridin-2-yl)quinazolin-4-yl]amine **573676-98-9P**, [4-[(2,5-Dimethylpyrrolidin-1-yl)sulfonyl]phenyl][7-(3-trifluoromethylpyridin-2-yl)quinazolin-4-yl]amine **573677-02-8P**, [4-[((2S)-2-Methoxymethylpyrrolidin-1-yl)sulfonyl]phenyl][7-(3-trifluoromethylpyridin-

2-yl)quinazolin-4-yl]amine **573677-04-0P**, [4-[((2R)-2-Methoxymethylpyrrolidin-1-yl)sulfonyl]phenyl][7-(3-trifluoromethylpyridin-2-yl)quinazolin-4-yl]amine **573680-38-3P**, [2-Pyrrolidin-1-ylmethyl-7-(3-trifluoromethylpyridin-2-yl)quinazolin-4-yl](4-trifluoromethylphenyl)amine **573680-84-9P**, [2-[2-(Pyrrolidin-1-yl)ethyl]-7-(3-trifluoromethylpyridin-2-yl)quinazolin-4-yl](4-trifluoromethylphenyl)amine **573681-61-5P**, (4-tert-Butylphenyl)[2-(pyrrolidin-1-ylmethyl)-7-(3-trifluoromethylpyridin-2-yl)quinazolin-4-yl]amine **573683-59-7P**, [2-[3-(Pyrrolidin-1-yl)propyl]-7-(3-trifluoromethylpyridin-2-yl)quinazolin-4-yl](4-trifluoromethylphenyl)amine **573685-18-4P**, [2-[[4-[2-(Pyrrolidin-1-yl)ethyl]piperazin-1-yl]methyl]-7-(3-trifluoromethylpyridin-2-yl)quinazolin-4-yl](4-trifluoromethylphenyl)amine **573686-42-7P**, [2-[6-(Pyrrolidin-1-yl)pyridin-3-yl]-7-(3-trifluoromethylpyridin-2-yl)quinazolin-4-yl](4-trifluoromethylphenyl)amine **573688-13-8P**, [2-Pyrrolidin-1-ylmethyl-7-(3-trifluoromethylpyridin-2-yl)quinazolin-4-yl](6-trifluoromethylpyridin-3-yl)amine **573688-67-2P**, [2-((S)-1-Propylpyrrolidin-2-yl)-7-(3-trifluoromethylpyridin-2-yl)quinazolin-4-yl](4-trifluoromethylphenyl)amine **573688-69-4P**, [2-((S)-Pyrrolidin-2-yl)-7-(3-trifluoromethylpyridin-2-yl)quinazolin-4-yl](4-trifluoromethylphenyl)amine
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate and receptor detector; preparation of substituted quinazolin-4-ylamine analogs as VR1 capsaicin receptor antagonists for relieving pain and for detecting receptors)

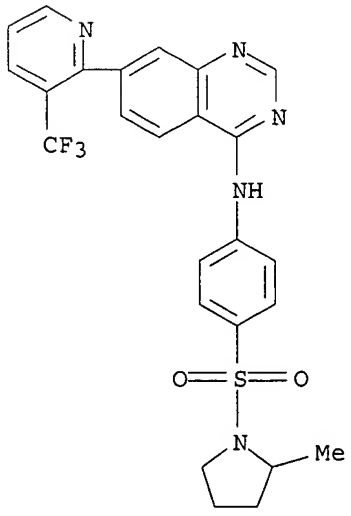
RN 573676-82-1 CAPLUS
CN Pyrrolidine, 1-[[4-[[7-[3-(trifluoromethyl)-2-pyridinyl]-4-quinazolinyl]amino]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



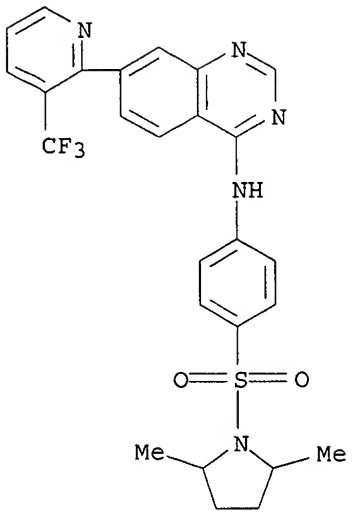
RN 573676-84-3 CAPLUS
CN 3-Pyrrolidinamine, N,N-dimethyl-1-[[4-[[7-[3-(trifluoromethyl)-2-pyridinyl]-4-quinazolinyl]amino]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 573676-96-7 CAPLUS
CN Pyrrolidine, 2-methyl-1-[[4-[[7-[3-(trifluoromethyl)-2-pyridinyl]-4-quinazolinyl]amino]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

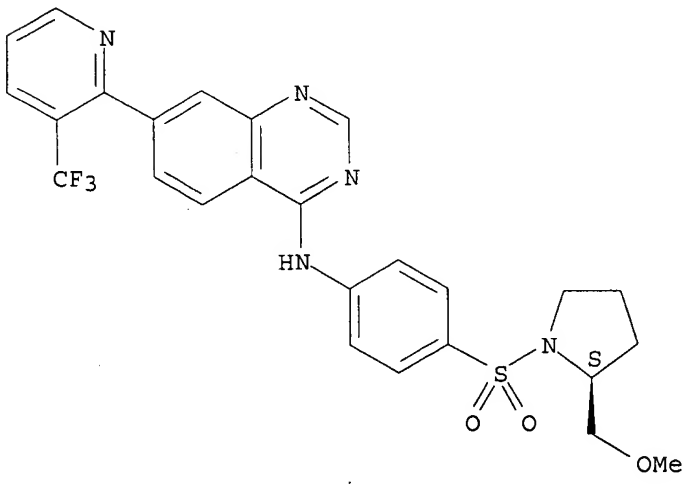


RN 573676-98-9 CAPLUS
CN Pyrrolidine, 2,5-dimethyl-1-[[4-[[7-[3-(trifluoromethyl)-2-pyridinyl]-4-quinazolinyl]amino]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



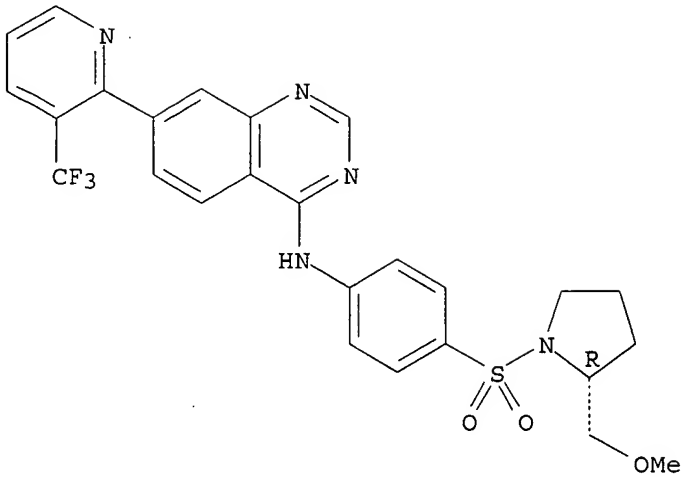
RN 573677-02-8 CAPLUS
CN Pyrrolidine, 2-(methoxymethyl)-1-[[4-[[7-[3-(trifluoromethyl)-2-pyridinyl]-4-quinazolinyl]amino]phenyl]sulfonyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

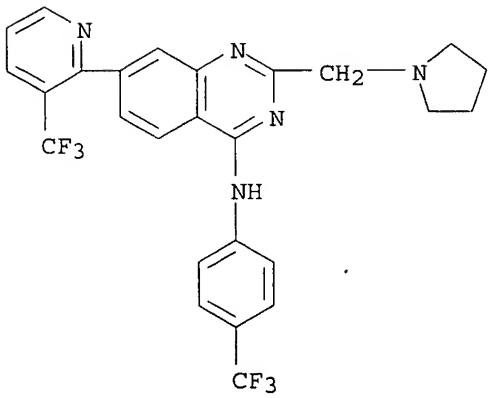


RN 573677-04-0 CAPLUS
CN Pyrrolidine, 2-(methoxymethyl)-1-[[4-[[7-[3-(trifluoromethyl)-2-pyridinyl]-4-quinazolinyl]amino]phenyl]sulfonyl]-, (2R)- (9CI) (CA INDEX NAME)

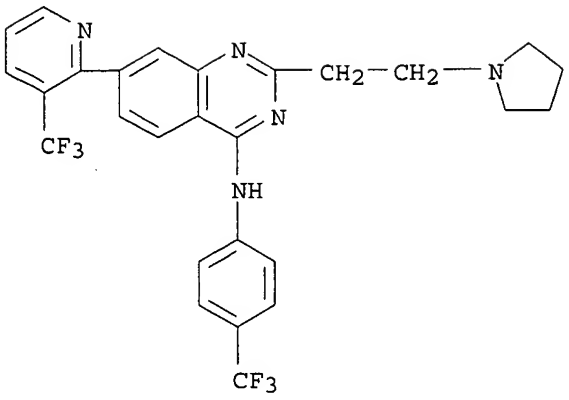
Absolute stereochemistry.



RN 573680-38-3 CAPLUS
CN 4-Quinazolinamine, 2-(1-pyrrolidinylmethyl)-N-[4-(trifluoromethyl)phenyl]-7-[3-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



RN 573680-84-9 CAPLUS
CN 4-Quinazolinamine, 2-[2-(1-pyrrolidinyl)ethyl]-N-[4-(trifluoromethyl)phenyl]-7-[3-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



RN 573681-61-5 CAPLUS
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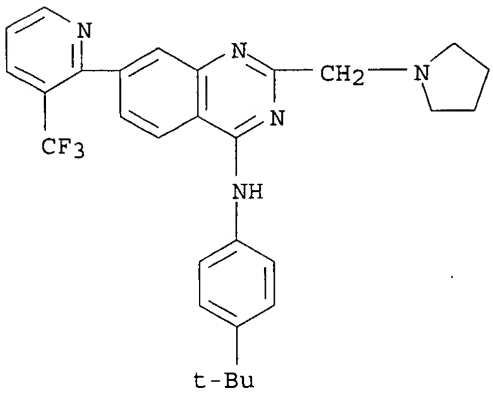
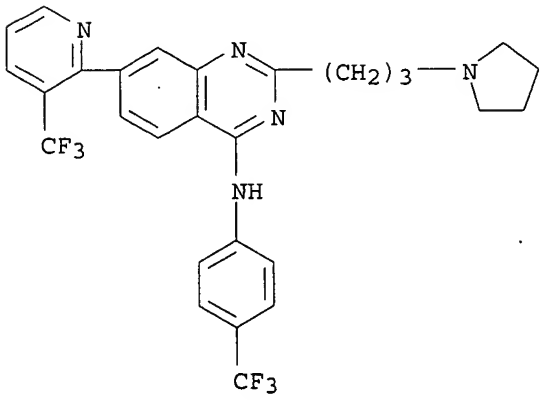
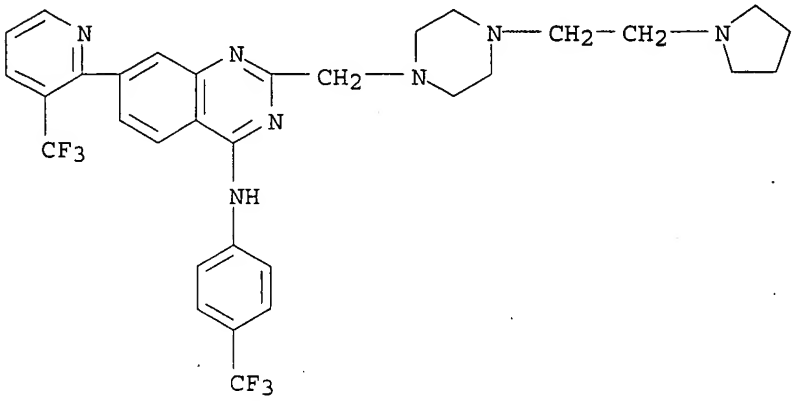


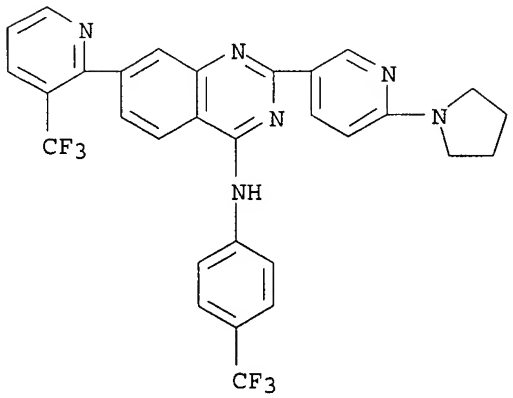
RN 573683-59-7 CAPLUS
CN 4-Quinazolinamine, 2-[3-(1-pyrrolidinyl)propyl]-N-[4-(trifluoromethyl)phenyl]-7-[3-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



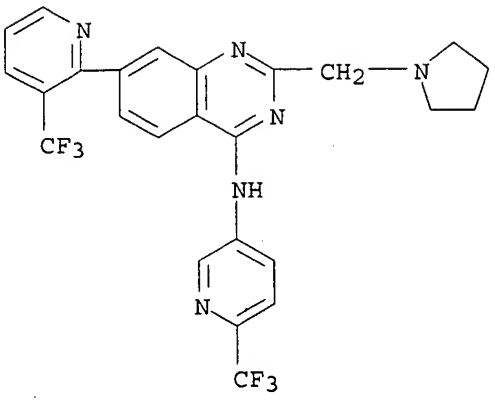
RN 573685-18-4 CAPLUS
CN 4-Quinazolinamine, 2-[[4-[2-(1-pyrrolidinyl)ethyl]-1-piperazinyl]methyl]-N-[4-(trifluoromethyl)phenyl]-7-[3-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



RN 573686-42-7 CAPLUS
CN 4-Quinazolinamine, 2-[6-(1-pyrrolidinyl)-3-pyridinyl]-N-[4-(trifluoromethyl)phenyl]-7-[3-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)

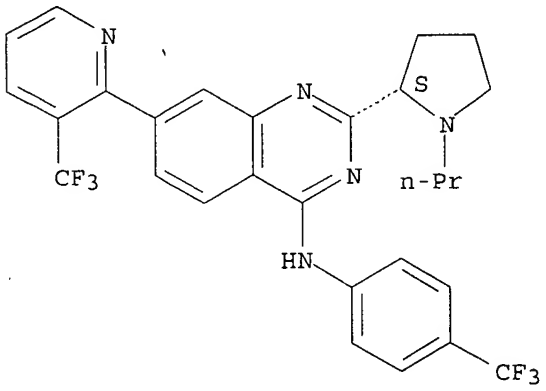


RN 573688-13-8 CAPLUS
CN 4-Quinazolinamine, 2-(1-pyrrolidinylmethyl)-7-[3-(trifluoromethyl)-2-pyridinyl]-N-[6-(trifluoromethyl)-3-pyridinyl]- (9CI) (CA INDEX NAME)



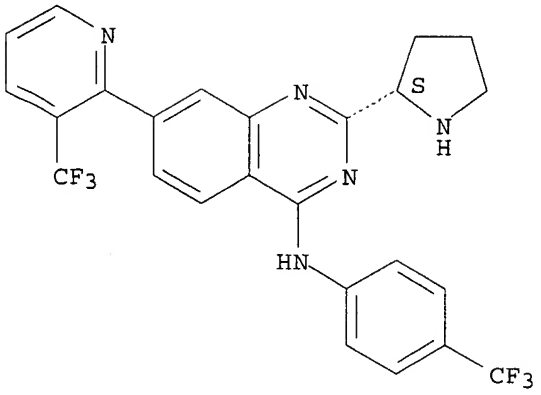
RN 573688-67-2 CAPLUS
CN 4-Quinazolinamine, 2-[(2S)-1-propyl-2-pyrrolidinyl]-N-[4-(trifluoromethyl)phenyl]-7-[3-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 573688-69-4 CAPLUS
CN 4-Quinazolinamine, 2-(2S)-2-pyrrolidinyl-N-[4-(trifluoromethyl)phenyl]-7-[3-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L75 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:935582 CAPLUS
DOCUMENT NUMBER: 136:69816
TITLE: Preparation of substituted 4-quinazolinamines for the treatment of abnormal cell growth
INVENTOR(S): Kath, John Charles; Bhattacharya, Samit Kumar; Morris, Joel
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001098277	A2	20011227	WO 2001-IB1046	20010614
WO 2001098277	A3	20020613		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2413424	AA	20011227	CA 2001-2413424	20010614
EP 1292591	A2	20030319	EP 2001-938484	20010614
EP 1292591	B1	20050202		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001011548	A	20030506	BR 2001-11548	20010614
JP 2004501139	T2	20040115	JP 2002-504233	20010614
EE 200200710	A	20040615	EE 2002-710	20010614
NZ 522568	A	20041224	NZ 2001-522568	20010614
AT 288431	E	20050215	AT 2001-938484	20010614
PT 1292591	T	20050630	PT 2001-938484	20010614
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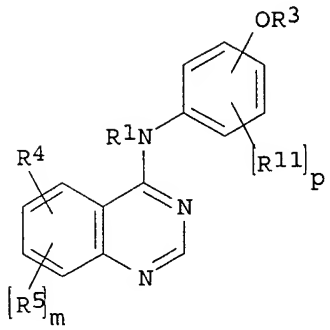
US 2002169165	A1	20021114	US 2001-883752	20010618
US 6890924	B2	20050510		

BG 107269	A	20030630	BG 2002-107269		20021112
ZA 2002010231	A	20040212	ZA 2002-10231		20021218
NO 2002006166	A	20021220	NO 2002-6166		20021220
US 2005159435	A1	20050721	US 2005-79648		20050314
PRIORITY APPLN. INFO.:			US 2000-213136P	P	20000622
			WO 2001-IB1046	W	20010614
			US 2001-883752	A3	20010618

OTHER SOURCE(S): MARPAT 136:69816

GI



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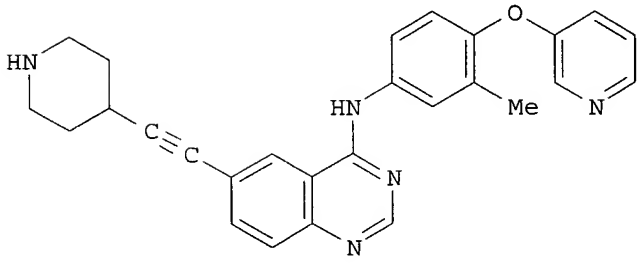


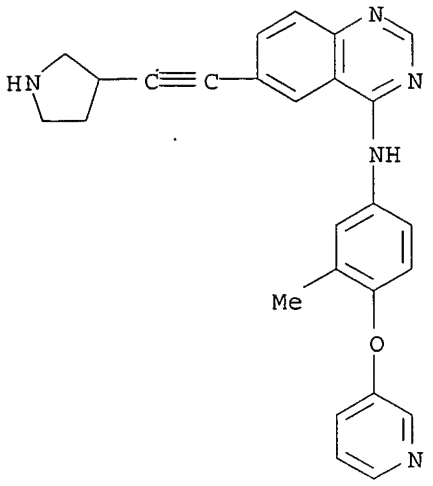
II

AB The title compds. [I; m = 0-3; p = 0-4; R1, R2 = H, alkyl; R3 = (CR1R2)t(4-10 membered heterocycle); t = 0-5; R4 = piperidin-4-ylethynyl, 3-(morpholin-4-yl)propenyl, 3-substituted-prop-1-ynyl, etc.; R5 = halo, OH, alkyl, etc.; R11 = halo, CN, NO2, etc.] and their pharmaceutically acceptable salts, useful for treating abnormal cell growth in mammals, were prepared Thus, alkylating 4-ethynylpiperidine-1-carboxylic acid tert-Bu ester with 4-chloro-6-iodoquinazoline followed by reacting the resulting 4-(4-chloroquinazolin-6-ylethynyl)-piperidine-1-carboxylic acid tert Bu ester with 3-methyl-4-(pyridin-3-yloxy)-phenylamine afforded II. The exemplified compds. I have IC50 of < 10 μM against erbB2 kinase.

IT **383433-01-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted 4-quinazolinamines for the treatment of abnormal cell growth)

RN 383433-01-0 CAPLUS

CN 4-Quinazolinamine, N-[3-methyl-4-(3-pyridinyloxy)phenyl]-6-(3-pyrrolidinylethynyl)- (9CI) (CA INDEX NAME)



=> s mattei p?/au;s mueller w?/au;s neidhart w?/au;s nettekoven m?/au;s pflieger p?/au

L76	63	FILE MEDLINE
L77	80	FILE BIOSIS
L78	66	FILE EMBASE
L79	55	FILE CAPLUS

TOTAL FOR ALL FILES

L80	264	MATTEI P?/AU

L81	440	FILE MEDLINE
L82	3463	FILE BIOSIS
L83	803	FILE EMBASE
L84	4709	FILE CAPLUS

TOTAL FOR ALL FILES

L85	9415	MUELLER W?/AU

L86	9	FILE MEDLINE
L87	27	FILE BIOSIS
L88	12	FILE EMBASE
L89	47	FILE CAPLUS

TOTAL FOR ALL FILES

L90	95	NEIDHART W?/AU

L91	7	FILE MEDLINE
L92	19	FILE BIOSIS
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TOTAL FOR ALL FILES

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L99          34 FILE CAPLUS

TOTAL FOR ALL FILES
L100         77 PFLIEGER P?/AU

=> s l80 and l85 and l90 and l95 and l100
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L102          2 FILE BIOSIS
L103          0 FILE EMBASE
L104          3 FILE CAPLUS

TOTAL FOR ALL FILES
L105          5 L80 AND L85 AND L90 AND L95 AND L100


=> dup rem l105
PROCESSING COMPLETED FOR L105
L106          5 DUP REM L105 (0 DUPLICATES REMOVED)

=> d 1-5 ibib abs;s *l80 or l85 or l90 or l95 or l100) and l69

L106 ANSWER 1 OF 5  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation  on STN
ACCESSION NUMBER:   2004:398066  BIOSIS
DOCUMENT NUMBER:    PREV200400402559
TITLE:              Quinoline derivatives.
AUTHOR(S):          Klug, Michael G. [Inventor, Reprint Author]; Mattei,
                    Patrizio [Inventor]; Mueller, Werner
                    [Inventor]; Neidhart, Werner [Inventor];
                    Nettekoven, Matthias Heinrich [Inventor];
                    Pflieger, Philippe [Inventor]; Plancher, Jean-Marc
                    [Inventor]
CORPORATE SOURCE:   Denver, CO, USA
                    ASSIGNEE: Hoffmann-La Roche Inc.
PATENT INFORMATION: US 6787558 20040907
SOURCE:             Official Gazette of the United States Patent and Trademark
                    Office Patents, (Sep 7 2004) Vol. 1286, No. 1.
                    http://www.uspto.gov/web/menu/patdata.html. e-file.
                    ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE:      Patent
LANGUAGE:           English
ENTRY DATE:         Entered STN: 13 Oct 2004
                    Last Updated on STN: 13 Oct 2004
AB   Compounds of formula I ##STR1## as well as pharmaceutically acceptable
     salts and esters thereof, wherein R1, R2, R3, A1 and A2 have the
     significance given in claim 1, can be used in the form of pharmaceutical
     preparations for the treatment or prevention of arthritis, cardiovascular
     diseases, diabetes, renal failure, eating disorders and obesity.

L106 ANSWER 2 OF 5  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation  on STN
ACCESSION NUMBER:   2004:175615  BIOSIS
DOCUMENT NUMBER:    PREV200400177681
TITLE:              Quinoline derivatives.
AUTHOR(S):          Mattei, Patrizio [Inventor, Reprint Author];
                    Mueller, Werner [Inventor]; Neidhart,
                    Werner [Inventor]; Nettekoven, Matthias
                    Heinrich [Inventor]; Pflieger, Philippe
                    [Inventor]
CORPORATE SOURCE:   Riehen, Switzerland
```

ASSIGNEE: Hoffmann-La Roche Inc.
PATENT INFORMATION: US 6696467 20040224
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Feb 24 2004) Vol. 1279, No. 4. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Mar 2004
Last Updated on STN: 31 Mar 2004

AB Compounds of general formula I ##STR1## as well as pharmaceutically acceptable salts and esters thereof, are potent inhibitors of neuropeptide Y and can be used in the form of pharmaceutical preparations for the treatment or prevention of various disease states and related morbidities including obesity.

L106 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:41451 CAPLUS
DOCUMENT NUMBER: 140:111423
TITLE: Quinazoline derivatives useful as neuropeptide Y (NPY) receptor ligands, particularly antagonists, their preparation and pharmaceutical compositions, and their use in the treatment of, e.g. obesity
INVENTOR(S): **Mattei, Patrizio; Mueller, Werner; Neidhart, Werner; Nettekoven, Matthias Heinrich; Pflieger, Philippe**
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004005265	A1	20040115	WO 2003-EP6868		20030627
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
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BR 2003012461	A	20050426	BR 2003-12461		20030627
EP 1560816	A1	20050810	EP 2003-740372		20030627
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2005535648	T2	20051124	JP 2004-518609		20030627
US 2004029901	A1	20040212	US 2003-613782		20030703
PRIORITY APPLN. INFO.:			EP 2002-14904	A	20020705
			WO 2003-EP6868	W	20030627

OTHER SOURCE(S): MARPAT 140:111423
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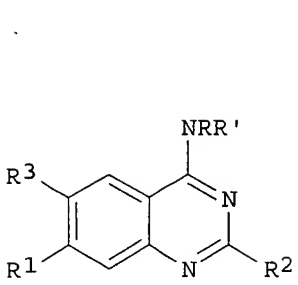

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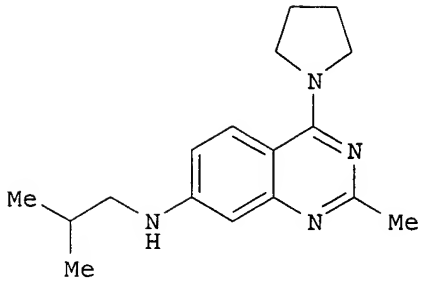

II

AB Title compds. I and their pharmaceutically acceptable salts and esters can be used in the form of pharmaceutical prepns. for the treatment or prevention of arthritis, cardiovascular diseases, diabetes, renal failure, eating disorders, and obesity [wherein: R1 = OR4 or NR5R6; = alkyl or amino; R3 = H, alkyl, or halogen; R4 = H, alkyl, alkoxyalkyl, hydroxyalkyl, aralkyl, heterocyclylalkyl, cycloalkylalkyl, amino-SO2-, or alkyl-SO2-; R5, R6 = H, alkyl, cycloalkyl, cycloalkylalkyl, alkylcarbonyl, cycloalkylcarbonyl, aryl, aralkyl, arylcarbonyl, alkoxyalkyl, hydroxyalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, alkyl-SO2-, aryl-SO2-, heterocyclyl-SO2-, or amino-SO2-; or NR5R6 = 5- to 10-membered heterocyclic ring with optional addnl. N or O atom, and optionally substituted with alkyl and/or alkoxy; NRR' = 5- to 7-membered saturated heterocyclic ring optionally containing a second heteroatom (O, N, or S)
and, optionally substituted by halogen, alkyl, alkoxy, haloalkoxy, cycloalkylalkoxy, hydroxy, amino, acetylamino, cyano, hydroxyalkyl, alkoxyalkyl, haloalkoxyalkyl, and cycloalkylalkoxyalkyl]. I are neuropeptide ligands; more specifically, they are selective neuropeptide Y (NPY) antagonists, and in particular, they are antagonists for the Y5 receptor subtype. Approx. 34 specific examples were prepared, and 10 of these are claimed. For instance, 4-bromoanthranilic acid was cyclocondensed with acetyl chloride to give 99.4% 7-bromo-2-methyl-3H-quinazolin-4-one, which was treated with POCl3 and PhNMe2 to give 59% 7-bromo-4-chloro-2-methylquinazoline. Aminolysis of this dihalide, first with pyrrolidine at the 4-position (100%), and then with isobutylamine at the 7-position, gave a preferred invention compound, II. In tests for displacement of labeled peptide YY (PYY) from mouse brain NPY5 receptors expressed in HEK 293 cells, compound II had an IC50 value of 3 nM.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L106 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:282396 CAPLUS

DOCUMENT NUMBER: 138:287536

TITLE: Preparation of 4-(heterocyclyl)quinolines as neuropeptide Y antagonists

INVENTOR(S): Klug, Michael G.; **Mattei, Patrizio**; **Mueller, Werner**; **Neidhart, Werner**; **Nettekoven, Matthias Heinrich**; **Pflieger, Philippe**; Plancher, Jean-marc

PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.

SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003028726	A1	20030410	WO 2002-EP10618	20020920
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US 2003158179	A1	20030821	US 2002-247009	20020919
US 6787558	B2	20040907		
CA 2460865	AA	20030410	CA 2002-2460865	20020920
EP 1432421	A1	20040630	EP 2002-779399	20020920
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BR 2002012929	A	20041013	BR 2002-12929	20020920
JP 2005508923	T2	20050407	JP 2003-532058	20020920
NO 2004001235	A	20040324	NO 2004-1235	20040324
ZA 2004002359	A	20050503	ZA 2004-2359	20040325
US 2004259858	A1	20041223	US 2004-896445	20040722
PRIORITY APPLN. INFO.:			EP 2001-123496 A	20010928
			US 2002-247009 A1	20020919
			WO 2002-EP10618 W	20020920

OTHER SOURCE(S): MARPAT 138:287536
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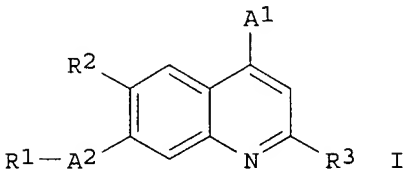

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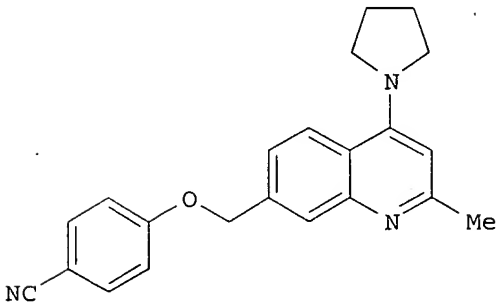

II

AB Title compds. I [wherein R1 = OR4 or NR5R6; R2 = H, (cyclo)alkyl, alkoxy, halo, heterocyclyl, or NH2; R3 = H, alkyl, NH2, or halo; R4 = H, alkyl,

aryl, aralkyl, cycloalkyl(alkyl), alkoxyalkyl, hydroxyalkyl, or heterocyclyl; R5 and R6 = independently H, alkyl, aryl, aralkyl, cycloalkyl(alkyl), alkoxyalkyl, hydroxyalkyl, or heterocyclyl; or NR5R6 = (un)substituted heterocyclyl; A1 = (un)substituted heterocyclyl; A2 = CH2 or CO; and pharmaceutically acceptable salts and esters thereof] were prepared as neuropeptide Y (NPY) antagonists. For example, reaction of 4-chloro-2-methylquinoline-7-carbonitrile with ethanolic HCl provided 4-chloro-2-methylquinoline-7-carboxylic acid Et ester (80%), which was reduced to the methanol derivative (71%) with diisobutylaluminum hydride in THF. Amination with pyrrolidine gave [2-methyl-4-(pyrrolidin-1-yl)quinolin-7-yl]methanol (90%). Coupling of the quinolinylmethanol with 4-fluorobenzonitrile afforded II. In radioligand competition binding assays using human embryonic kidney cells transfected with recombinant mouse NPY5-receptor, II exhibited activity as an NPY5 antagonist with IC50 of 22 nM. Thus, I are useful for the treatment or prevention of arthritis, cardiovascular diseases, diabetes, renal failure, eating disorders, and obesity (no data).

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L106 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:633280 CAPLUS
DOCUMENT NUMBER: 139:179984
TITLE: Preparation of quinoline derivatives as neuropeptide inhibitors
INVENTOR(S): **Mattei, Patrizio; Mueller, Werner; Neidhart, Werner; Nettekoven, Matthias Heinrich; Pflieger, Philippe**
PATENT ASSIGNEE(S): Hoffmann-La Roche Inc., Switz.
SOURCE: U.S. Pat. Appl. Publ., 27 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003153553	A1	20030814	US 2003-358006	20030204
US 6696467	B2	20040224		
CA 2473181	AA	20030814	CA 2003-2473181	20030127
WO 2003066055	A1	20030814	WO 2003-EP777	20030127
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1474145	A1	20041110	EP 2003-702533	20030127
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BR 2003007441	A	20050104	BR 2003-7441	20030127
JP 2005523901	T2	20050811	JP 2003-565479	20030127
PRIORITY APPLN. INFO.:			EP 2002-1967 A	20020204
			WO 2003-EP777 W	20030127

OTHER SOURCE(S): MARPAT 139:179984

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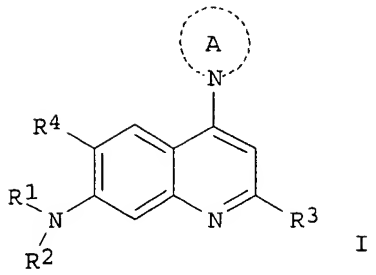

I

AB Compds. of general formula (I) as well as pharmaceutically acceptable salts and esters thereof [R1, R2 = H, alkyl, cycloalkyl, cycloalkylalkyl, alkylcarbonyl, cycloalkylcarbonyl, cycloalkylalkylcarbonyl, aryl, aralkyl, arylcarbonyl, aralkylcarbonyl, alkoxyalkyl, hydroxyalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, heterocyclylalkylcarbonyl, carbocyclyl, carbocyclylalkyl, amino, alkyl-SO2-, aryl-SO2-, heterocyclyl-SO2-, SO2NH2; or R1 and R2 together with the N atom to which they are attached form a 5- to 10-membered heterocyclic ring which optionally comprises a second heteroatom selected from nitrogen or oxygen and wherein the heterocyclyc ring is optionally substituted with one or more substituents independently selected from the group consisting of alkyl and alkoxy; R3 = H, alkyl, NH2, halo; R4 = H, halogen, heterocyclyl, NH2, alkyl; A = a 5 to 7-membered saturated heterocyclic ring comprising the nitrogen atom which is attached to the quinoline ring and optionally a second heteroatom which is selected from oxygen, sulfur or nitrogen and, wherein the ring A is optionally substituted by one to three substituents independently selected from the group consisting of alkyl, alkoxy, hydroxy, amino, acetylamino, cyano, hydroxyalkyl, alkoxyalkyl, cycloalkylalkoxy, and cycloalkylalkoxyalkyl] are prepared These compds. are potent inhibitors of neuropeptide Y and can be used in the form of pharmaceutical prepns. to reduce appetite for the treatment or prevention of various disease states and related morbidities including obesity. Thus, a suspension of 1.01 g (3 mmol) 7-iodo-2-methyl-4-pyrrolidin-1-ylquinoline, 0.186 g (0.3 mmol) racemic BINAP, 33.7 mg (0.15 mmol) palladium(II) acetate, and 0.87 g (9 mmol) sodium tert-butylate in toluene (25 mL) was treated at room temperature with 0.427 g (6 mmol) aminomethylcyclopropane and then heated to reflux under an argon atmospheric for 20 h to give, after workup and silica gel chromatog., 253 mg (30%) cyclopropylmethyl(2- methyl-4-pyrrolidin-1-ylquinolin-7-yl)amine as light yellow foam. Isobutyl(2-methyl-4-pyrrolidin-1-ylquinolin-7-yl)amine and furan-2-carboxylic acid (2-methyl-4-pyrrolidin-1-ylquinolin-7-yl)amide showed IC50 of 0.7 and 0.3 nM, resp., for inhibiting the binding of [125I]peptide YY to recombinant mouse NPY5-receptor expressed in human embryonic kidney 293 cells (HEK293).

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=> s (l80 or l85 or l90 or l95 or l100) and l69
L107          0 FILE MEDLINE
L108          0 FILE BIOSIS
L109          0 FILE EMBASE
L110          1 FILE CAPLUS

TOTAL FOR ALL FILES
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Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

L111 1 (L80 OR L85 OR L90 OR L95 OR L100) AND L69

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L111 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:41451 CAPLUS
DOCUMENT NUMBER: 140:111423
TITLE: Quinazoline derivatives useful as neuropeptide Y (NPY) receptor ligands, particularly antagonists, their preparation and pharmaceutical compositions, and their use in the treatment of, e.g. obesity
INVENTOR(S): **Mattei, Patrizio; Mueller, Werner; Neidhart, Werner; Nettekoven, Matthias Heinrich; Pflieger, Philippe**
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004005265	A1	20040115	WO 2003-EP6868	20030627
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BR 2003012461	A	20050426	BR 2003-12461	20030627
EP 1560816	A1	20050810	EP 2003-740372	20030627
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US 2004029901	A1	20040212	US 2003-613782	20030703
PRIORITY APPLN. INFO.:			EP 2002-14904 A	20020705
			WO 2003-EP6868 W	20030627

OTHER SOURCE(S): MARPAT 140:111423
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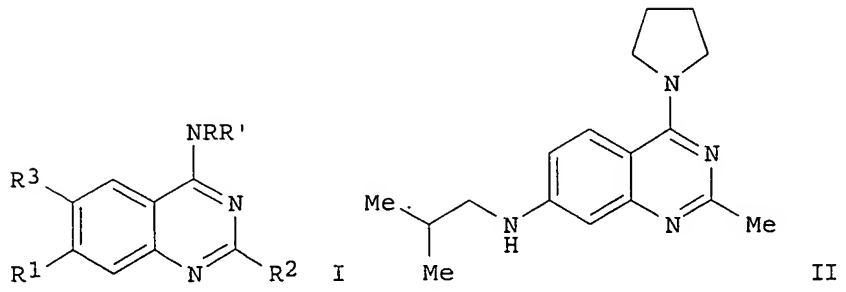


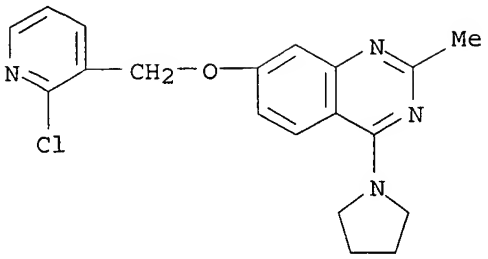
Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

AB Title compds. I and their pharmaceutically acceptable salts and esters can be used in the form of pharmaceutical prepns. for the treatment or prevention of arthritis, cardiovascular diseases, diabetes, renal failure, eating disorders, and obesity [wherein: R1 = OR4 or NR5R6; = alkyl or amino; R3 = H, alkyl, or halogen; R4 = H, alkyl, alkoxyalkyl, hydroxyalkyl, aralkyl, heterocyclylalkyl, cycloalkylalkyl, amino-SO2-, or alkyl-SO2-; R5, R6 = H, alkyl, cycloalkyl, cycloalkylalkyl, alkylcarbonyl, cycloalkylcarbonyl, aryl, aralkyl, arylcarbonyl, alkoxyalkyl, hydroxyalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, alkyl-SO2-, aryl-SO2-, heterocyclyl-SO2-, or amino-SO2-; or NR5R6 = 5- to 10-membered heterocyclic ring with optional addnl. N or O atom, and optionally substituted with alkyl and/or alkoxy; NRR' = 5- to 7-membered saturated heterocyclic ring optionally containing a second heteroatom (O, N, or S)
and, optionally substituted by halogen, alkyl, alkoxy, haloalkoxy, cycloalkylalkoxy, hydroxy, amino, acetylamino, cyano, hydroxyalkyl, alkoxyalkyl, haloalkoxyalkyl, and cycloalkylalkoxyalkyl]. I are neuropeptide ligands; more specifically, they are selective neuropeptide Y (NPY) antagonists, and in particular, they are antagonists for the Y5 receptor subtype. Approx. 34 specific examples were prepared, and 10 of these are claimed. For instance, 4-bromoanthranilic acid was cyclocondensed with acetyl chloride to give 99.4% 7-bromo-2-methyl-3H-quinazolin-4-one, which was treated with POCl3 and PhNMe2 to give 59% 7-bromo-4-chloro-2-methylquinazoline. Aminolysis of this dihalide, first with pyrrolidine at the 4-position (100%), and then with isobutylamine at the 7-position, gave a preferred invention compound, II. In tests for displacement of labeled peptide YY (PYY) from mouse brain NPY5 receptors expressed in HEK 293 cells, compound II had an IC50 value of .3 nM.

IT **646450-58-0P**, 7-(2-Chloropyridin-3-ylmethoxy)-2-methyl-4-pyrrolidin-1-ylquinazoline **646450-62-6P**, 7-(2-Fluoropyridin-3-ylmethoxy)-2-methyl-4-pyrrolidin-1-ylquinazoline **646450-69-3P**, (S)-[1-[7-(2-Chloropyridin-3-ylmethoxy)-2-methylquinazolin-4-yl]pyrrolidin-2-yl]methanol **646450-80-8P**, (**Isobutyl**)[2-**methyl**-4-(**pyrrolidin**-1-yl)**quinazolin**-7-yl]**amine** **646450-86-4P**, [2-**Methyl**-4-(**pyrrolidin**-1-yl)**quinazolin**-7-yl](**pyridin**-3-yl)**amine** **646450-87-5P**, **Furan**-2-**carboxylic acid** N-[2-**methyl**-4-(**pyrrolidin**-1-yl)**quinazolin**-7-yl]**amide** **646450-88-6P**, (S)-[4-(3-Ethoxypyrrolidin-1-yl)-2-methylquinazolin-7-yl](pyridin-3-yl)amine **646450-90-0P**, (S)-[4-(3-Methoxypyrrolidin-1-yl)-2-methylquinazolin-7-yl](pyridin-3-yl)amine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of **quinazoline** derivs. as NPY antagonists for treatment of obesity, etc.)

RN 646450-58-0 CAPLUS

CN Quinazoline, 7-[(2-chloro-3-pyridinyl)methoxy]-2-methyl-4-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



RN 646450-62-6 CAPLUS
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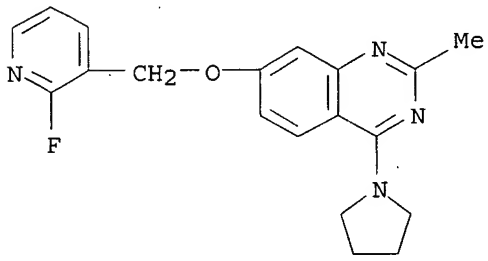
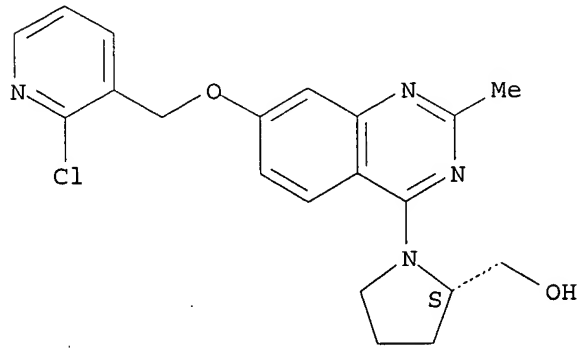
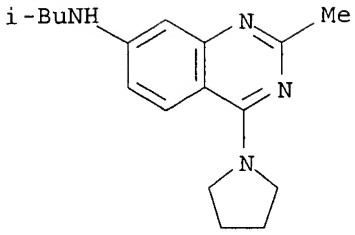


RN 646450-69-3 CAPLUS
CN 2-Pyrrolidinemethanol, 1-[7-[(2-chloro-3-pyridinyl)methoxy]-2-methyl-4-quinazolinyl]-, (2S)- (9CI) (CA INDEX NAME)

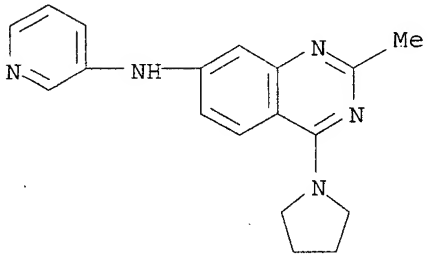
Absolute stereochemistry.



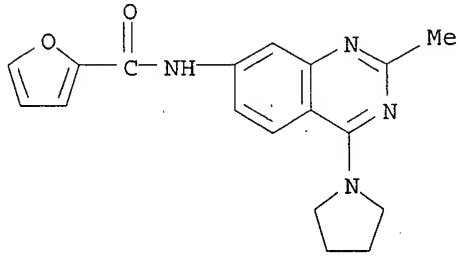
RN 646450-80-8 CAPLUS
CN 7-Quinazolinamine, 2-methyl-N-(2-methylpropyl)-4-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



RN 646450-86-4 CAPLUS
CN 7-Quinazolinamine, 2-methyl-N-3-pyridinyl-4-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)

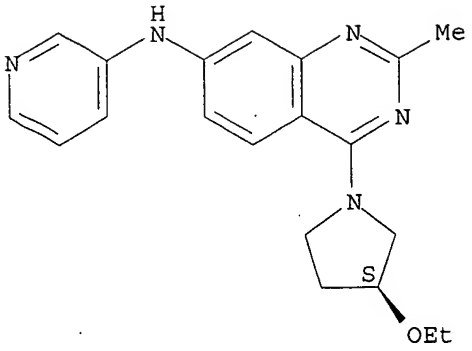


RN 646450-87-5 CAPLUS
CN 2-Furancarboxamide, N-[2-methyl-4-(1-pyrrolidinyl)-7-quinazolinyl]- (9CI) (CA INDEX NAME)



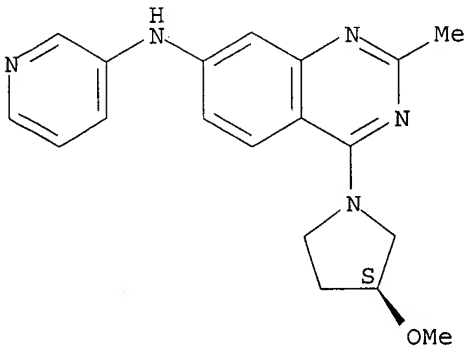
RN 646450-88-6 CAPLUS
CN 7-Quinazolinamine, 4-[(3S)-3-ethoxy-1-pyrrolidinyl]-2-methyl-N-3-pyridinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 646450-90-0 CAPLUS
CN 7-Quinazolinamine, 4-[(3S)-3-methoxy-1-pyrrolidinyl]-2-methyl-N-3-pyridinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> dis his

(FILE 'HOME' ENTERED AT 10:57:04 ON 29 NOV 2005)

FILE 'REGISTRY' ENTERED AT 10:57:13 ON 29 NOV 2005
L1 STR
L2 2 S L1
L3 39 S L1 FUL

FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS' ENTERED AT 10:59:48 ON 29 NOV 2005
L4 0 FILE MEDLINE
L5 0 FILE BIOSIS
L6 0 FILE EMBASE
L7 4 FILE CAPLUS
TOTAL FOR ALL FILES
L8 4 S L3

FILE 'REGISTRY' ENTERED AT 11:00:18 ON 29 NOV 2005
E "4-(2-METHYL-4-PYRROLIDIN-1-YL-QUINAZOLIN-7-YLOXYMETHYL)-BENZ

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

```
                E "7-(2-CHLORO-PYRIDIN-3-YLMETHOXY)-2-METHYL-4-PYRROLIDIN-1-YL-
L9            0 S METHYL(L)PYRROLIDIN?(L)QUINAZOLIN?(L)OXYMETHYL(L)BENZONITRILE
L10           0 S METHYL(L)PYRROLIDIN?(L)QUINAZOLIN?(L)YLOXYMETHYL(L)BENZONITRI
L11           1 S CHLORO(L)PYRIDIN?(L)YLMETHOXY(L)METHYL(L)PYRROLIDIN?(L)QUINAZ
L12           1 S FLUORO(L)PYRIDIN?(L)YLMETHOXY(L)METHYL(L)PYRROLIDIN?(L)QUINAZ
L13           1 S CHLORO(L)PYRIDIN?(L)YLMETHOXY(L)METHYL(L)QUINAZOLIN?(L)PYRROL
L14           0 S ETHOXY(L)PYRROLIDIN?(L)METHYL(L)QUINAZOLIN?(L)YLOXYMETHYL(L)B
L15           1 S ISOBUTYL(L)METHYL(L)PYRROLIDIN?(L)QUINAZOLIN?(L)AMINE
L16          41 S METHYL(L)PYRROLIDIN?(L)QUINAZOLIN?(L)PYRIDIN?(L)AMINE?
L17           1 S FURAN(L)CARBOXYLIC ACID(L)METHYL(L)PYRROLIDIN?(L)QUINAZOLIN?(
L18           9 S ETHOXY(L)PYRROLIDIN?(L)METHYL(L)QUINAZOLIN?(L)PYRIDIN?(L)AMIN
L19          14 S METHOXY(L)PYRROLIDIN?(L)METHYL(L)QUINAZOLIN?(L)PYRIDIN?(L)AMI

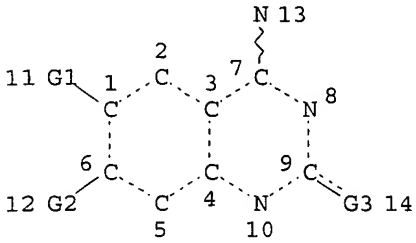
     FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS' ENTERED AT 11:07:00 ON 29 NOV 2005
L20           1 FILE MEDLINE
L21           0 FILE BIOSIS
L22           1 FILE EMBASE
L23           8 FILE CAPLUS
     TOTAL FOR ALL FILES
L24          10 S METHOXY(L)PYRROLIDIN?(L)METHYL(L)QUINAZOLIN?(L)PYRIDIN?(L)AMI
L25           0 FILE MEDLINE
L26           0 FILE BIOSIS
L27           0 FILE EMBASE
L28           6 FILE CAPLUS
     TOTAL FOR ALL FILES
L29           6 S ETHOXY(L)PYRROLIDIN?(L)METHYL(L)QUINAZOLIN?(L)PYRIDIN?(L)AMIN
L30           0 FILE MEDLINE
L31           0 FILE BIOSIS
L32           0 FILE EMBASE
L33           1 FILE CAPLUS
     TOTAL FOR ALL FILES
L34           1 S FURAN(L)CARBOXYLIC ACID(L)METHYL(L)PYRROLIDIN?(L)QUINAZOLIN?(
L35           1 FILE MEDLINE
L36           0 FILE BIOSIS
L37           1 FILE EMBASE
L38          14 FILE CAPLUS
     TOTAL FOR ALL FILES
L39          16 S METHYL(L)PYRROLIDIN?(L)QUINAZOLIN?(L)PYRIDIN?(L)AMINE? OR L16
L40           0 FILE MEDLINE
L41           0 FILE BIOSIS
L42           0 FILE EMBASE
L43           1 FILE CAPLUS
     TOTAL FOR ALL FILES
L44           1 S ISOBUTYL(L)METHYL(L)PYRROLIDIN?(L)QUINAZOLIN?(L)AMINE OR L15
L45           0 FILE MEDLINE
L46           0 FILE BIOSIS
L47           0 FILE EMBASE
L48           0 FILE CAPLUS
     TOTAL FOR ALL FILES
L49           0 S ETHOXY(L)PYRROLIDIN?(L)METHYL(L)QUINAZOLIN?(L)YLOXYMETHYL(L)B
L50           0 FILE MEDLINE
L51           0 FILE BIOSIS
L52           0 FILE EMBASE
L53           1 FILE CAPLUS
     TOTAL FOR ALL FILES
L54           1 S CHLORO(L)PYRIDIN?(L)YLMETHOXY(L)METHYL(L)QUINAZOLIN?(L)PYRROL
L55           0 FILE MEDLINE
L56           0 FILE BIOSIS
L57           0 FILE EMBASE
L58           1 FILE CAPLUS
```

```
     TOTAL FOR ALL FILES
L59           1 S FLUORO(L)PYRIDIN?(L)YLMETHOXY(L)METHYL(L)PYRROLIDIN?(L)QUINAZ
L60           0 FILE MEDLINE
L61           0 FILE BIOSIS
L62           0 FILE EMBASE
L63           1 FILE CAPLUS
     TOTAL FOR ALL FILES
L64           1 S CHLORO(L)PYRIDIN?(L)YLMETHOXY(L)METHYL(L)PYRROLIDIN?(L)QUINAZ
L65           1 FILE MEDLINE
L66           0 FILE BIOSIS
L67           1 FILE EMBASE
L68          14 FILE CAPLUS
     TOTAL FOR ALL FILES
L69          16 S L24 OR L29 OR L34 OR L39 OR L44 OR L54 OR L59 OR L64
L70           1 FILE MEDLINE
L71           0 FILE BIOSIS
L72           1 FILE EMBASE
L73          13 FILE CAPLUS
     TOTAL FOR ALL FILES
L74          15 S L69 NOT L8
L75          14 DUP REM L74 (1 DUPLICATE REMOVED)
L76          63 FILE MEDLINE
L77          80 FILE BIOSIS
L78          66 FILE EMBASE
L79          55 FILE CAPLUS
     TOTAL FOR ALL FILES
L80         264 S MATTEI P?/AU
L81         440 FILE MEDLINE
L82        3463 FILE BIOSIS
L83         803 FILE EMBASE
L84        4709 FILE CAPLUS
     TOTAL FOR ALL FILES
L85        9415 S MUELLER W?/AU
L86           9 FILE MEDLINE
L87          27 FILE BIOSIS
L88          12 FILE EMBASE
L89          47 FILE CAPLUS
     TOTAL FOR ALL FILES
L90          95 S NEIDHART W?/AU
L91           7 FILE MEDLINE
L92          19 FILE BIOSIS
L93          13 FILE EMBASE
L94          38 FILE CAPLUS
     TOTAL FOR ALL FILES
L95          77 S NETTEKOVEN M?/AU
L96           9 FILE MEDLINE
L97          25 FILE BIOSIS
L98           9 FILE EMBASE
L99          34 FILE CAPLUS
     TOTAL FOR ALL FILES
L100         77 S PFLIEGER P?/AU
L101          0 FILE MEDLINE
L102          2 FILE BIOSIS
L103          0 FILE EMBASE
L104          3 FILE CAPLUS
     TOTAL FOR ALL FILES
L105          5 S L80 AND L85 AND L90 AND L95 AND L100
L106          5 DUP REM L105 (0 DUPLICATES REMOVED)
L107          0 FILE MEDLINE
L108          0 FILE BIOSIS
```

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

```
L109            0 FILE EMBASE
L110            1 FILE CAPLUS
     TOTAL FOR ALL FILES
L111            1 S (L80 OR L85 OR L90 OR L95 OR L100) AND L69

=> d l3 que stat
L1                STR
```




```
VAR G1=X/AK/H
VAR G2=O/N
VAR G3=C/N
NODE ATTRIBUTES:
NSPEC   IS R      AT  13
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  14

STEREO ATTRIBUTES: NONE
L3              39 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED   12672 ITERATIONS                          39 ANSWERS
SEARCH TIME: 00.00.01


=> log y
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              206.63     693.69

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                 ENTRY    SESSION
CA SUBSCRIBER PRICE                              -12.41     -15.33

STN INTERNATIONAL LOGOFF AT 11:14:24 ON 29 NOV 2005
```